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ANNUAL REVIEW

Annual review of selected scientific literature: Report of the committee on scientific investigation of the American Academy of Restorative Dentistry

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ABSTRACT

Statement of problem. It is clear the contemporary dentist is confronted with a blizzard of information regarding materials and techniques from journal articles, advertisements, newsletters, the internet, and continuing education events. While some of that information is sound and helpful, much of it is misleading at best.

Purpose. This review identifies and discusses the most important scientific findings regarding outcomes of dental treatment to assist the practitioner in making evidence-based choices. This review was conducted to assist the busy dentist in keeping abreast of the latest scientific information regarding the clinical practice of dentistry.

Material and methods. Each of the authors, who are considered experts in their disciplines, was asked to peruse the scientific literature published in 2015 in their discipline and review the articles for important information that may have an impact on treatment decisions. Comments on experimental methodology, statistical evaluation, and overall validity of the conclusions are included in many of the reviews.

Results. The reviews are not meant to stand alone but are intended to inform the interested reader about what has been discovered in the past year. The readers are then invited to go to the source if they wish more detail.

Conclusions. Analysis of the scientific literature published in 2015 is divided into 7 sections, dental materials, periodontics, prosthodontics, occlusion and temporomandibular disorders, sleep-disordered breathing, cariology, and implant dentistry. (J Prosthet Dent 2016;116:663-740)

This review was conducted to assist the busy dentist in keeping abreast of the latest scientific information regarding the clinical practice of dentistry. Each of the authors, who are considered experts in their disciplines, was asked to review the scientific literature published in 2015 in their discipline and review the articles for important information that may have an impact on treatment decisions. Comments on experimental methodology, statistical evaluation, and overall validity of the conclusions are included in many of the reviews. The reviews are not meant to stand alone but are intended to inform the interested reader about what has been discovered in the past year. The readers are then invited to go to the source if they wish more detail.

It is clear the contemporary dentist is confronted with a blizzard of information regarding materials and techniques from journal articles, advertisements, newsletters, the internet, and continuing education events. Although some of that information is sound and helpful, much of it is misleading at best. This review identifies and discusses the most important scientific findings and

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outcomes of dental treatment to assist the practitioner in making evidence-based choices.

One area of interest is the increased publishing of systematic reviews and meta-analyses. Although these can be of great interest to both academic and clinical dentists, let the reader beware! Usually the authors of these systematic reviews indicate the quality or lack of quality of the clinical trials included in the review, but often they do not. A systematic review of poorly conducted clinical trials often may provide misleading results. Readers are encouraged to use one of the several available tools and checklists to evaluate systematic reviews and their conclusions.

The analysis of the scientific literature published in 2015 is divided into 7 sections: (1) dental materials, (2) periodontics, (3) prosthodontics, (4) occlusion and temporomandibular disorders, (5) sleep-disordered breathing, (6) cariology, and (7) implant dentistry.

DENTAL MATERIALS

Restoration repair and replacement

The National Dental Practice-Based Research Network published 3 papers related to a common investigation of patterns and outcomes of direct restorations that had been either repaired or replaced. The investigation used an initial survey questionnaire phase of clinical scenarios followed consecutively by a patient and restoration clinical design. Network dentists (195) provided repair or replacement of 5889 defective restorations with subsequent 12-month evaluations. The first paper described the concordance between how practitioners decided between repair and replacement in hypothetical scenarios and their actual clinical decision patterns.[1] The conclusions were that decisions based upon the survey scenarios were typically concordant with how they practiced. Those who chose repair over replacement more often in the hypothetical scenarios were more likely to repair restorations in their clinical practice. The second paper investigated factors that influenced a practitioner's decision to repair or replace a defective restoration.[2] Factors that influence the decision to repair included the dentist having placed the original restoration and the restoration being on a molar tooth. When dentists who placed the original restoration decided to replace a restoration, that decision was most significantly influenced by the restoration being an amalgam and when the defect was a fracture. The third paper reported outcomes of the repairs and replacements.[3] Of the 5889 defective restorations available for follow-up, 1498 (25%) were repairs and 4391 (75%) were replacements. Of these, 378 (6%) experienced subsequent failures, 7% of repairs failed, and 5% of replacements failed. Subsequent failure was also significantly more likely if the restorations were on a molar but surprisingly was not related to the number of surfaces of the restoration. Failure was also noted as being more likely in large group practice settings than in solo or small group settings. One outcome that the authors emphasized was the severity of treatment required for failed repairs versus replacements. It was stated that repaired restorations were less likely to require replacement, endodontic treatment, or extraction than those that had been replaced. It is important to understand that the major limitation of the design of this study is the lack of treatment randomization. Dentists determined the need to either repair or replace based upon their professional and personal decision criteria. Therefore a great deal of bias was likely present in the assignment of treatment. Dentists would naturally select repair for restorations and teeth with a lesser likelihood of future complications and select replacement whenever outcomes were judged to be less predictable. Thus, it is difficult to imply with these results that the outcomes of repaired restorations will be more favorable than replacements.

Another practice-based network study assessed patient perceived and clinically assessed outcomes of both repaired and replaced defective restorations.[4] In this study of 103 patients, those who received repairs reported less pretreatment anxiety, had shorter treatment times, and used less local anesthetic, and repairs were associated with less caries depth. Although none of this comes as a surprise, it should be pointed out that this also was a dentists-assigned treatment model with considerable inherent selection bias.

In contrast, there were 2 papers that evaluated the 10-year outcomes of defective amalgam and composite resin restorations that were randomly assigned to either repair or replacement. The first tracked 50 composite resin restorations that were randomly assigned to either repair or replacement.[5] The restorations were scored by 2 blinded examiners who used modified United States Public Health Service (USPHS) criteria and were found to behave similarly with regard to margin adaptation, secondary caries, anatomy, and color. The second study examined similar parameters in 60 defective amalgam restorations (20 in each group) randomly assigned to be sealed, replaced, or left untreated.[6] Forty-four restorations were available for 10-year evaluation, and no differences were observed between sealed and replaced amalgam with respect to margin adaptation and tooth sensitivity, whereas replaced restorations fared better with respect to margin staining. All 3 groups of restorations showed similar levels of degradation over time, but nearly all were considered clinically acceptable. These results continue to confirm the potential value of repairing direct restorations, but barriers remain in the clinical decision process and economic drivers.

Sealants and infiltration

Several papers and systematic reviews in 2015 evaluated the clinical outcomes of pit and fissure sealants and infiltrating resins. One paper investigated the epidemiologic trends in caries and use of sealants among third-grade children in the state of New York.[7] Third-grade oral examination surveys from 2002 to 2004 were compared with those conducted between 2009 and 2012 with respect to caries experience, untreated caries, sealant prevalence, and preventive behavior. The good news was that between these 2 periods, caries experience decreased from 54.1% to 45.2%, whereas untreated caries dropped from 33.0% to 23.6%. Over this same time, the prevalence of sealants increased from 16.7% to 36.0%. The authors noted that, although a measureable improvement had occurred overall, these improvements were not uniform across subgroups and that disease prevalence among low-income children remained high.

An evidence-based review of pediatric restorative and preventive strategies evaluated the literature between 1995 and 2013 to determine the effectiveness of incomplete caries removal, pit and fissure sealants, and resin infiltration.[8] Evidence was graded as "strong," "evidence in favor," or "expert opinion" by consensus of the authors. They concluded that there was "strong" evidence of restoration of teeth with incomplete caries excavation, resulting in fewer post-treatment adverse events than complete excavation. Also graded as "strong" was the evidence that sealants should be used on pits and fissures judged to be at risk for caries. The same was true for sealing surfaces that already exhibited noncavitated lesions. The evidence regarding infiltration was considered "evidence in favor" but only as it related to improving the appearance of white spot lesions.

Two additional reviews examined the resin infiltration for managing proximal decay. The first was a systematic review that included 4 studies, 1 in high caries risk and 3 in moderate and low caries risk in adolescents and adults.[9] All studies were randomized, split-mouth designs with proper blinding, but study sizes only ranged from 22 to 48 participants. All 4 studies showed significant differences in caries progression between treated and control/placebo groups, indicating that infiltration was effective at arresting the progression of noncavitated lesions.

The second systematic review resulted in inclusion of 8 trials, again all using split-mouth designs.[10] Six evaluated infiltration in permanent teeth and 2 in primary teeth. All studies used lesion progression as their primary outcome. Seven of the 8 studies were judged to be at high risk of bias due to lack of blinding of both participants and study personnel. A meta-analysis of pooled data showed that the microinvasive infiltration significantly reduced the odds of lesion progression (odds ratio [OR]=0.24; 95% confidence interval [CI]=0.14 to 0.41). No adverse events were reported, and the quality of the evidence was graded as moderate. The conclusions of this review were that microinvasive treatment was more effective than fluoride varnish or hygiene advice in arresting noncavitated lesions. The authors pointed out, however, that the number of studies is still small, and other factors, such as cost-benefit, have not been considered.

For sealants, 1 paper reported a randomized controlled trial evaluating the effect of fluoride-releasing sealants on adjacent proximal tooth surfaces.[11] First permanent molars were sealed with either a glass ionomer, a fluoride-releasing resin-based sealant, or a resin-based sealant without fluoride. Treatments were randomly assigned among 2767 children, and sealant retention and D1 to D3 caries were assessed on the proximal surface of the adjacent primary molar. Results showed that the prevalence of surfaces affected by caries was significantly lower in the glass ionomer and fluoride-releasing sealant groups and that the fewest new lesions were formed in the glass ionomer sealant group. This was despite the observation that partial sealant loss was highest in the glass ionomer sealant group.

A final systematic review evaluated the effect of adhesive method on the retention of pit and fissure sealants.[12] Five studies were included in a meta-analysis comparing the retention of sealants following use of self-etch and conventional acid etching, with or without the application of an additional adhesive. The findings favored conventional acid etching, regardless of whether an additional adhesive was used in conjunction with the sealant. Self-etch adhesives demonstrated the lowest rate of sealant retention.

Silver compounds

Two systematic reviews were published assessing literature related to silver diamine fluoride. The first review provided a general review of nonsurgical methods for arresting or slowing the progression of dentin caries in the primary teeth of preschool children.[13] These methods included topical forms of fluoride, sealants, resin infiltration, xylitol, chlorhexidine, ozone, and remineralizing compounds. Thirty-three papers were included in the review, resulting in only 4 studies with clinical data. Three of these studies reported arrest of dentin caries in preschool children using silver diamine fluoride, and 1 reported that daily brushing with 1000-ppm fluoride toothpaste in a kindergarten setting stabilized the caries progression. The overall conclusion was that there was as-yet limited evidence to support the effectiveness of silver diamine fluoride and that more well-designed randomized controlled trials were required to confirm this trend.

A second mapping of systematic reviews examined the evidence for both primary and secondary prevention

of caries using professional and self-care interventions.[14] Thirty-nine reviews were rated using the GRADE scale into 4 levels of quality. The quality of evidence was considered high for primary caries prevention using fluoride toothpaste, and quality was moderate using fluoride varnish and sealants. The quality for primary prevention using fluoride gel, fluoride mouth rinse, xylitol gums, and silver diamine fluoride were considered low. For secondary caries prevention and caries arrest, only fluoride varnish and silver diamine fluoride provided consistent benefits, although the quality of this evidence was still considered low. The consistency of results that continues to be cited for silver diamine fluoride provides hope that higher quality studies will eventually confirm its effectiveness.

One in situ study examined the mechanism of remineralization of early carious lesions, comparing silver diamine fluoride to glass ionomer.[15] A double-blind crossover design used enamel slabs attached to orthodontic brackets to expose artificially induced enamel lesions to either treatment for 28 days. Mineral density and depth of change were measured before and after treatment exposure by using microcomputed tomography. The net positive changes in mineral density were similar for both silver diamine fluoride and glass ionomer and significantly higher than untreated controls. The glass ionomer appeared to remineralize to a greater depth, but this difference was not significant. This study confirms that one of the primary mechanisms for silver diamine fluoride is the stimulation of remineralization, rather than only an antimicrobial agent.

There were also several papers reporting the use of nanoparticles of silver as the antimicrobial and anticaries material additive. One cell culture study evaluated the antimicrobial activity of silver nanoparticles between *Streptococcus mutans* and *S. mutans* biofilms.[16] Exposure to 100 ppm of the nanoparticles resulted in a 2.3 log reduction in *S. mutans* colony-forming units, and smaller particles appeared to have a greater effectiveness with lower effective concentrations. One caveat was that concentrations above 10 ppm also showed cytotoxic effects upon human fibroblast cells. The value of such single-line cell culture tests in evaluating potential toxicity, however, is questionable.

A clinical evaluation of silver nanoparticles was reported for a randomized, double-blind controlled trial with 130 carious primary teeth in 60 children.[17] This trial recorded probe penetration of carious dentin over a period of 12 months in teeth that had been randomly assigned to either the topical application of a silver nanoparticle solution or water. The progression of active caries as assessed by a blunt explorer was considered a failure. At the end of 12 months, the combined exfoliation and failure rate for the nanoparticle treatment was 33%, while the water control was 65%, which was statistically significant. The nanoparticle solution was noted to effectively harden and arrest caries in the primary teeth but with the added benefit of not causing the black staining associated with silver diamine fluoride.

A second clinical study examined incorporation of silver nanoparticles into the baseplates of orthodontic appliances.[18] This study was a double-blind randomized trial with crossover of nanoparticle containing appliances and non-nanoparticle control appliances. The results showed that the nanoparticle-containing appliances reduced salivary levels of cariogenic bacteria by 2- to 70-fold. Silver nanoparticles continue to show promise as a caries preventative and control strategy, and it will be interesting to follow this technology going forward.

Xylitol

The literature was rich with studies and reviews of xylitol in 2015. Three reviews focused on the impact of the maternal use of xylitol on infant levels of *S. mutans*. The first study attempted to use a random effects model to assess the relative risks of *S. mutans* infection in saliva or plaque of children 6 to 24 months of age.[19] Eleven randomized controlled trials were included consisting of 601 mother/child pairs. The results showed that the incidence of *S. mutans* in infant saliva or plaque was significantly reduced at all ages, indicating a reduction in mother-child transmission. A second similar review by a different group of authors chose the same studies and thankfully arrived at the same conclusions,[20] a phenomenon not often experienced in the dental literature. A third systematic review of clinical trials resulted in only 2 trials that fulfilled the stricter inclusion criteria, and these authors concluded that there was "a dearth of current evidence" supporting the use of xylitol in expectant mothers to reduce levels of *S. mutans* in their children.[21] So much for consistency.

A number of studies reported on effectiveness of xylitol therapy in children and adults. One report from the Xylitol for Adult Caries Trial tracked 8084 tooth surfaces in 543 caries-active adults.[22] Some of the more interesting data was the natural progression of the disease over time, where, for noncavitated lesions, half of them reversed, and only 8.3% progressed to cavitation or restoration. Xylitol showed no significant effect on the progression of either noncavitated or cavitated lesions.

A more extensive systematic review was published in the Cochrane Database, which assessed effectiveness of xylitol in both adults and children.[23] Ten randomized controlled trials with 5903 participants were included, with only 1 study considered low risk of bias and 7 being of high risk of bias. The main finding was that over 2.5 to 3 years of use, a fluoride toothpaste containing 10% xylitol may reduce caries by 13% in children compared with a fluoride-only toothpaste, but this evidence was

considered low quality. The remaining evidence was insufficient to determine any benefit from various xylitol products in any age group. Only 4 studies reported adverse events, although none was associated with the xylitol-containing toothpaste. Adverse events included mouth sores, cramps, bloating, constipation, flatulence, loose stool, diarrhea, and similar contributors to a really bad day.

A clinical study compared the effects of 2 chewing gums, 1 containing casein phosphopeptide-amorphous calcium phosphate and the other containing xylitol, on salivary *S. mutans* levels.[24] The study used 60 dental students chewing gum 3 times daily for 3 weeks. Both of the treatments were effective at reducing *S. mutans* levels, with the calcium phosphate gum having a slight edge over the xylitol gum. Unfortunately, there was no nontherapeutic control gum included in this study, and they are still trying to clean the dried gum from the underside of the dental school desks.

Another comparison of xylitol, herbal, and control gums in 72 school children had them chewing 4 times daily for 21 days.[25] At the end of this period, the gum containing 100% xylitol sweetener showed a significant reduction in *S. mutans*, while neither the herbal nor the control gums were effective. A third study comparing xylitol chewing gum, chewable tablets, and no treatment controls was carried out using 41 participants undergoing orthodontic treatment.[26] Plaque scores and bacterial counts were tracked for 12 months with xylitol showing no clinical or antiplaque benefit over the no-treatment control.

Two studies were great examples of how multiple confounders can muddy the waters in clinical designs. The first study investigated community dwelling older adults in a 2-year randomized design with multiple interventions including tailored hygiene instruction, dry mouth relief, reduced sugar exposure frequency, topical fluorides, antimicrobial agents, professional tooth cleaning, and some xylitol products.[27] Not surprisingly, everyone's oral health improved, and the improvement could not be attributed to any one particular intervention.

A similar situation occurred in a study of 562 elementary school children who were randomly assigned to daily exposure to 7.8 g of xylitol in gummy bears or placebo gummy bears. Both of the groups also received oral health education, tooth brushing with fluoridated paste, topical fluoride, fluoride varnish, and dental sealants.[28] Again, it is not surprising with all of these confounders that no additional benefit could be attributed to the xylitol consumption.

As the earlier reported reviews have pointed out, evidence for the effectiveness of xylitol continues to be weak, the number of available clinical studies are small, and the quality of the evidence is consistently poor, a combination that is far too common in the dental literature.

Composite resin

Some of the more interesting papers relating to composite resin restorations centered on the evaluation of specific techniques and longer-term performance. It is fortunate that many of the early clinical trials have been able to maintain recall and are starting to provide more long-term evidence. Among the papers on technique was an in vivo study of the performance of different matrix systems on proximal contour and contacts.[29] Studies like this are often performed using in vitro simulations, but this evaluation used clinically placed restorations. In this study, 3 different examiners evaluated the proximal contour after placement with radiographs and contact quality using floss. Ten restorations were placed in each group, using a flat metal matrix/wood wedge, a precontoured sectional metal matrix with an elastic wedge, or a polyester strip with a reflective wedge. The precontoured matrix system produced 9 of 10 correct contours, whereas the flat metal and polyester matrices produced only 8 of 20 correct contours. Contact adequacy was acceptable for all 3 systems.

Another technique paper compared the 18-year survival of posterior composite resin restorations placed with or without a glass ionomer base.[30] A total of 632 restorations placed in 97 patients within a single dental practice were tracked for up to 18 years after placement. Annual failure rates were not statistically different for restorations with (1.9%) and without (2.1%) glass ionomer base. A significant weakness of this study was that the restorations were not originally randomly assigned the use of the base. One interesting aspect was that, although failures were equivalent, the reasons for failures were differently distributed, with composite resin fractures being more predominant in the glass ionomer-based restoration. This phenomenon could easily be the product of selection bias with the lack of randomization.

A third technique paper evaluated the 10-year performance of composite resin restorations that had been refurbished (not completely replaced).[31] This study followed 52 restorations in 26 participants. Restorations selected for refurbishing showed clinical features rated at "bravo" in the USPHS criteria, and restorations rated clinically acceptable at alfa or bravo were assigned as untreated controls. Both of the groups showed measurable deterioration over 10 years, but no differences were found in survival between refurbished and untreated controls. The clinical characteristics were similar for both groups, with most properties rated as acceptable after 10 years of clinical service.

One paper reported on the performance of composite resin used for closure of midline diastemata.[32] This study followed 45 patients over 60 months and found that 91%

had been retained for the entire 60 months. At 60 months, 62% had no noticeable color difference from the adjacent tooth, and 73% had no signs of gingival inflammation. These restorations had no or minimal functional loading.

One clinical study and 1 systematic review addressed the use of composite resin for managing anterior tooth wear. The clinical trial followed 1010 direct composite resin restorations in 164 patients placed by 1 clinician with up to 8 years of follow-up.[33] Most restorations were placed on maxillary anterior teeth, and the composite resin used was a hybrid (Spectrum; Dentsply DeTrey). The failure rate in the first year after placement was 5.4%, with higher failure rates noted in the mandibular arch, in edge-to-edge incisal relationships, and when there was a lack of posterior occlusal support. The failure rate over the average 33.8 months of service was 9.6% for mandibular anterior teeth and 6% for maxillary anterior teeth.

A systematic review of attrition that did not yet include the above-mentioned study identified 3 prospective and 2 retrospective studies that included 772 direct and indirect anterior restorations in 100 patients.[34] Early survival rates were high but dropped to 50% after 5 years of service. It was noted that in 91% of anterior restorations where composite resin was used to increase the vertical dimension of occlusion, the posterior occlusion had reestablished within 18 months. The overall conclusion was that the use of anterior composite resin restorations to increase vertical dimension can only provide short to medium-term management of tooth wear.

From a performance perspective, 1 interesting paper examined the life course of proximal tooth surfaces adjacent to newly placed class II composite resins. This practice-based network study done in Norway evaluated 750 surfaces, either sound or with early enamel lesions, that were in contact with the composite resins over an average of 4.9 years.[35] Of those initially sound enamel surfaces (n=417), 38.8% remained sound, 34.0% developed enamel caries, and 27.2% developed caries into dentin. In enamel surfaces with initial lesions (n=333), 57.3% remained in the enamel, and 42.7% progressed into dentin. Significant risk factors for initially sound surfaces included inadequate oral hygiene (OR=1.53; CI=1.10 to 3.68), higher initial DMFT (OR=1.12; 95% CI=1.04 to 1.20), maxillary teeth (OR=2.01; 95% CI=1.14 to 3.56), and interestingly, surfaces on the right side of the mouth (OR=1.65; 95% CI=1.01 to 2.72). For surfaces with initial enamel lesions, the significant risk factor for dentin caries was higher initial DMFT (OR=1.06; 95% CI=1.00 to 1.13). As has been shown before, the most reliable predictor of caries progression is caries history, and the importance of recall and follow-on prevention is evident.

Two systematic reviews evaluated the longevity of posterior composite resin restorations. The first review identified 18 studies who met the inclusion criteria, of whom 8 were included in the analysis.[36] Among these studies, the overall incidence rate for failure was 1.55 restorations per 100 restoration years. The most common biological reasons for failure were caries followed by fracture of the restoration. Unfortunately, the quality of the overall evidence was rated as low.

The second review identified 88 prospective studies for a meta-analysis.[37] The observation periods varied from 1 to 17 years, while most were not beyond 5 years. In the first 5 years, the most common modes of failure in descending order were restoration fracture, caries, and margin failures. No distinction could be made between different brands of materials, and the mean annual failure rate for short studies (<5 years) was 1.46% and 1.97% for longer-term studies. One interesting finding was that failure rates decreased with increasing recall rate, indicating that selection bias with regard to access and dental awareness is inherent in these types of studies.

No discussion of composite resin would be complete without mentioning polymerization shrinkage. Two papers that studied polymerization shrinkage are worth noting. The first study was a 15-year comparison of a reduced shrinkage stress composite with a conventional microhybrid material.[38] This was an intraindividual comparison with 50 patients receiving at least 1 pair of class II restorations, one being randomly assigned to either a reduced shrinkage composite resin (InTen-S) or a microhybrid (Point 4; Kerr Corp) and the other restoration to the alternate material. Both of the materials were placed with the same adhesive system for a total of 106 restorations, 73 in molars and 33 in premolars. The restorations were subsequently evaluated using USPHS criteria. Amazingly, there were 91 restorations to evaluate over the 15 years. At 15 years, the overall success rate was 77%, with nearly an equal number of failures in both materials. Annual failure rates were consistent with those of other studies at 1.5% for the reduced shrinkage and 1.6% for the microhybrid. Again, the main reasons for failure were caries and composite resin fracture. The conclusion was that the low shrinkage composite resin presented good clinical performance but not significantly better than the control microhybrid.

A review of the literature related to polymerization shrinkage arrived at a supporting conclusion.[39] This review investigated both laboratory and clinical evidence for polymerization shrinkage stress in composite resins. The authors concluded that although there is considerable evidence for the presence of contraction stress, there is little if any direct evidence of the clinical effects of these stresses. No direct evidence exists that demonstrates that contraction stresses reduce clinical longevity. Once again, it appears we are relying upon indirect evidence without

corroborating clinical support to guide huge investments in material development and product promotion.

Amalgam

Fewer papers relating to amalgam appear in the literature each year, and almost all publications center around the study of potential mercury toxicity from amalgam restorations. One noteworthy study examined the impact of in utero exposure to mercury on the nervous system development of sons of Swedish dental personnel.[40] Sons of 1690 female dentists and 10 420 dental assistants were compared with cohorts of sons of other female health care personnel. Analyses were stratified by decade of birth to account for the decline in use of amalgam during the study period. The analysis found no risk elevation for neurological disease, epilepsy, or intellectual disability for sons of dental personnel during any decade. There was no support for the hypothesis that mercury exposure in Swedish dentistry during the 1960s, 1970s, or 1980s had any effect on the sons of female dental personnel.

Another study of dental personnel reported on the contributions of both elemental and organic mercury as parts of total body burden.[41] Dietary and occupational exposure patterns were determined for 630 dental professionals attending an American Dental Association meeting. Blood, urine, and hair samples were analyzed to determine possible correlations between exposure patterns and measured levels of both organic and elemental Hg. Results showed that the number of personal amalgam restorations, years in practice, number of amalgams placed, working hours, and sex predicted urinary elemental mercury levels. Organic mercury levels in blood and hair were predicted by fish consumption, with most of the intake coming from 5 species (swordfish, fresh tuna, white canned tuna, whitefish, and king mackerel).

A similar study of children 9 to 14 years of age compared amalgam and dietary exposure to urinary and hair levels of mercury.[42] Results confirmed that levels of elemental Hg in urine were related to the number of amalgam restorations and organic levels in hair to fish consumption. These results demonstrated the importance of measuring all sources of exposure when assessing exposure to mercury.

A study of the association of amalgam fillings with *Helicobacter pylori* infection and the bacteria's reaction to treatment was reported.[43] The title of the paper used the term "impact" to describe the relationship, but studies of this type are only capable of reporting associations, and one must keep in mind that systems as complicated as the gut biome are impacted by a huge number of environmental factors. The investigators compared the rates of *H. pylori* infections between cohorts with and without amalgam restorations and also subjected those with infection to 3 different regimens of treatment. The main finding was that the frequency of *H. pylori* infection was lower in the cohort with amalgam (53.7%) than in the cohort with no amalgam (78.8%). There were small differences in responses to treatment between cohorts that were of minimal clinical significance.

Another paper reported on the association between dental amalgam fillings and Alzheimer's disease by using a health insurance database in Taiwan.[44] A sample of just over 200 000 individuals over 65 years of age were assessed over 5 years for positive diagnosis of Alzheimer's. Overall, 2.76% of men exposed to amalgam had a history of Alzheimer's diagnosis, whereas 2.8% of unexposed men were diagnosed. For women, 2.73% of amalgam-exposed individuals were diagnosed with Alzheimer's disease, while 2.93% of their unexposed counterparts were positive. What is interesting is that despite this population-level trend, when adjustments were made for age, sex, income, and residential region, the OR for risk was reversed, showing a slightly higher risk for Alzheimer's with amalgam (OR=1.07 for men and 1.132 for women). This demonstrates how dependent associations can be upon extraneous environmental factors and how overlooking potential factors can impact statistical outcomes. As an example, in this study, there was no knowledge of the history of amalgam exposure, other sources of mercury, or exposure to other heavy metals in any of these individuals.

Additionally, each year, there is at least one paper that just leaves you scratching your head. Just when you thought it was safe to use your cell phone again, an article on the increased release of mercury from dental amalgam exposed to electromagnetic fields warns that this may lead to a "paradigm shift" in evaluating the health effects of amalgam.[45] The authors claim that exposure to electromagnetic fields from devices like cell phones increases the release of mercury from fillings and can present a health hazard to individuals who are especially susceptible, such as pregnant women. When reviewing the data for which this was based, however, no health effects were ever measured, and the miniscule levels of increase that were reported would never be expected to result in any type of adverse health outcome. This publication left many unanswered questions, but multiple attempts to contact the authors by text message or cell phone were unsuccessful.

Endodontic materials

Most papers related to endodontic materials continued to focus on different applications of mineral trioxide aggregate (MTA). As more clinical studies are published, we are beginning to see more systematic reviews and meta-analyses in the literature. One study of direct pulp capping compared MTA with 3 other materials, including calcium hydroxide, Biodentine (Septodont), and Single

Bond Universal (3M ESPE).[46] The authors reported good reparative dentin formation with the MTA, the calcium hydroxide, and the Biodentine but poor repair with the adhesive. These results must be viewed with caution, however, as this study was done on mechanical exposures in healthy third molars and not on diseased teeth as would be encountered in most clinical situations.

A second paper reported on the outcomes of a 2-stage MTA pulp-capping procedure on 64 teeth with deep carious lesions.[47] The 2 stages were caries excavation with MTA and provisional placement at 1 appointment followed later by placement of a definitively bonded composite resin restoration. No comparison or control materials were included, but the overall success rate after an average service of 3.6 years was 91.3%. Success rates were also higher for teeth with occlusal caries than for proximal caries, for teeth with initial caries versus recurrent and for patients younger than 40 years of age.

A meta-analysis was also published on the effectiveness of MTA and calcium hydroxide for direct pulp capping.[48] Thirteen studies met the inclusion criteria, and in randomized controlled trials, MTA showed a significantly higher success rate over calcium hydroxide (OR=2.26; 95% CI=1.33 to 3.85; *P*=.003). MTA also had a better success rate than calcium hydroxide in retrospective nonrandomized trials (OR=2.88; 95% CI=1.86 to 4.44; *P*<.001).

An updated systematic review of pulp capping and partial pulpotomy included 22 articles and noted that since the original review in 2006, the quality of studies has improved, which is encouraging.[49] The overall conclusions were that limited evidence shows that both calcium hydroxide and MTA produce hard tissue barriers in direct pulp capping situations, whereas adhesives and enamel matrix derivatives do not.

Other applications of MTA were also reported. One study reported on pulpotomies in primary molar teeth, but it is not referenced here because evaluations were only carried out until 6 months after treatment. A systematic review reported on treatment outcomes of nonsurgical repair of root perforations.[50] Seventeen studies were included and 12 were subjected to meta-analysis with results showing a 72.5% overall success rate with all materials. MTA appeared to have a higher success rate than other materials at 80.9%; other factors associated with higher success were maxillary teeth and teeth with no preexisting radiolucency adjacent to the perforation.

Two papers reported on use of MTA as root-end filling materials.[51,52] Although both of the studies reported success rates as high as >80%, neither provided comparative controls against other filling materials. Last, 2 papers with fairly well-designed studies compared MTA with calcium hydroxide for apexification of immature permanent teeth. The first randomly assigned 40 open-apex incisors to MTA or calcium hydroxide filling using either ultrasonic placement or hand placement of the filling material.[53] The method of placement had little bearing on outcomes, but it was interesting to note that, although MTA resulted in more rapid apexification, calcium hydroxide resulted in greater elongation of the root length during apexification. Perhaps faster is not necessarily better. The second study on apexification made a similar random assignment of 30 nonvital permanent incisors and, after 12 months, noted that radiographically 50% of the calcium hydroxide teeth exhibited hard tissue barriers, whereas 82.4% of the MTA-treated teeth did so, although the significance level for this difference was *P*=.07.[54] This study did not report on differences in root elongation.

One paper of particular interest provided a cost-effectiveness comparison for direct pulp capping, comparing MTA with calcium hydroxide.[55] Cost-effectiveness analyses are few and far between in the dental literature, and this one modeled a treated permanent molar in a 20-year-old patient over a typical lifetime by using Markov models. The primary outcomes were tooth retention and costs, including the direct pulp capping costs as well as actuarial estimates of typical restored tooth lifetime costs. The MTA direct pulp cap was more effective from both a tooth retention and lifetime cost perspective (lifetime=52 years, costs=1368 Euros [$1536 USD]) than the calcium hydroxide (lifetime=49 years, costs=1527 Euros [$1714 USD]). This is one of those exceedingly rare situations in health care where a new technology actually provides improved outcomes at a lower cost.

Glass ionomers

The cariostatic potential of glass ionomer materials was studied in 1 randomized controlled trial and 2 literature reviews in 2015. The randomized clinical trial was a large study of 2776 children, in whom permanent first molars were sealed with either a high-viscosity glass ionomer cement, a fluoride-releasing resin-based sealant, or a resin-based sealant without fluoride.[11] Both the sealed teeth and the adjacent primary molars were followed for 30 months to assess sealant retention and caries development. The prevalence of caries was found to be significantly lower in both the glass ionomer and the fluoride-releasing resin-sealed molars, as well as fewer caries on the distal surfaces of the primary second molars. Partial sealant loss was higher for the glass ionomer sealant, but overall, both of the fluoride-releasing materials demonstrated an ability to protect both the treated and the adjacent surfaces.

A related systematic review evaluated the ability of glass ionomer to prevent caries in adjacent proximal surfaces.[56] Ten articles were included, 6 laboratory studies and 4 longitudinal clinical trials. In the clinical

trials, no protective effect could be verified; however, the meta-analysis of laboratory data showed a significant protective ability for glass ionomer. This review did not include the above described trial and once again highlights the frequent inconsistency between laboratory and clinical data.

A second systematic review and meta-analysis examined secondary caries inhibition in occlusal and occlusoproximal glass ionomer restorations.[57] Eight studies were included, and the conclusions were that secondary caries rates did not improve over control materials in occlusal restorations but were significantly lower in occlusoproximal restorations (OR=1.7; 95% CI=1.2 to 2.5). Overall, the evidence continues to lean toward the ability of glass ionomer materials to inhibit secondary and adjacent caries.

One very interesting study evaluated glass ionomer restorations placed using atraumatic restorative treatment (ART) in carious lesions of elderly patients.[58] Ninety-nine independently living adults 65 to 90 years of age were randomly assigned to either the ART or the conventional restorations and followed over 2 years. At 2 years, 96 ART and 121 conventional restorations were available for assessment, of the 300 restorations originally placed. The cumulative survival rates after 2 years were 85.4% for ART and 90.9% for conventional restorations, which were not significantly different. The viability of this treatment option is encouraging in view of the critical need to address dental disease within this growing demographic.

PERIODONTICS

This year's review covered topics relating to the assessment, prevalence, and treatment regimens of periodontal disease, the systemic conditions affecting periodontal health, periodontal regeneration, use of lasers in periodontal therapy, soft tissue augmentation adjacent to teeth and implants, alveolar ridge preservation and augmentation techniques, and periimplantitis.

Periodontal disease assessment, prevalence, and treatment

The prevalence, severity, and extent of periodontitis in the US adult population using data from the most recent (2009 to 2012) National Health and Nutrition Examination Survey (NHANES) continues to demonstrate the widespread prevalence of periodontal disease.[59] In this study, estimates were derived for dentate adults, ≥30 years of age, from the US civilian, noninstitutionalized population. Periodontitis was defined by combinations of clinical attachment loss (attachment loss) and periodontal probing depth from 6 sites per tooth on all teeth, except for third molars, using standard surveillance case definitions. For the first time in NHANES history, sufficient numbers of non-Hispanic Asians were sampled from 2011 to 2012 to provide reliable estimates of their periodontitis prevalence. This report found that, from 2009 to 2012, 46% of US adults, representing 64.7 million people, had periodontitis, with 8.9% having severe periodontitis. Overall, 3.8% of all periodontal sites (10.6% of all teeth) had pocket depth ≥4 mm, and 19.3% of sites (37.4% teeth) had attachment loss ≥3 mm. Periodontitis prevalence was positively associated with increasing age and was higher among men. Periodontitis prevalence was highest in Hispanics (63.5%) and non-Hispanic blacks (59.1%), followed by non-Hispanic Asian Americans (50.0%), and was lowest in non-Hispanic whites (40.8%). Prevalence varied 2-fold between the lowest and highest levels of socioeconomic status, whether defined by poverty or by education. This study confirmed a high prevalence of periodontitis in US adults ≥30 years of age, with almost 50% affected.

Untreated periodontal disease may result in tooth loss. Although tooth replacement strategies may include dental implant therapies, the use of conventional fixed partial dental prostheses (FDPs) frequently remains a viable, cost-effective, and stable treatment option. Di Febo et al[60] conducted a long-term cohort study to evaluate the efficacy and complications of FDPs in a sample of 100 patients with periodontal disease who were treated and maintained 20 years after placement of the FDPs. After active treatment, including periodontal surgery and endodontic and prosthetic treatment, patients were enrolled in a supportive periodontal care (SPC) program with 3- to 6-month recalls. All patients showed clinical data recorded at the original consultation (T0), the first SPC visit following the completion of prosthetic treatment (T1), and at the latest SPC clinical session 20 years after T1 (T2). Multivariate analyses were performed to investigate the influence of clinical variables on the risk of prosthetic abutment (PA) loss after 20 years. At T1, a total of 948 PAs represented the original sample of experimental teeth. At the 20-year follow-up, a total of 854 PAs (90.1%) were still in function, while 94 PAs (9.9%) in 41 patients (41%) were lost during SPC; 98% of lost PA were endodontically treated. Vertical root fracture (48%) was the major cause of PA loss, while progression of periodontitis caused 31% of PA loss. Age, full-mouth plaque score, full-mouth bleeding score, and oral parafunctions were associated with increased probability of PA failure. Among clinically related factors, endodontic treatment, root resection/amputation, multirooted teeth, and abutments associated with parafunction were associated with increased risk of abutment loss after 20 years. This study suggests that perioprosthetic treatment in compliant patients is highly successful after 20 years of high-quality SPC.

Opening of the proximal contact between an implant-supported prosthesis and the natural dentition may result

in food impaction and worsening of the periodontal status. Two studies examined this problem. In the first study, food impaction and periodontal/periimplant tissue conditions were evaluated in relation to the embrasure dimensions between implant-supported FDPs and adjacent teeth.[61] A total of 215 embrasures of 150 FDPs in 100 patients were included in the study. Clinical assessments of the periodontal/periimplant mucosal conditions, radiographic assessments of embrasure dimensions, and overall patient satisfaction were used as explanatory variables for the food impaction and periodontal/periimplant tissue conditions adjacent to implant-supported FDPs. Food impaction was reported in 96 of 215 embrasures (44.7%) between implant-supported FDPs and adjacent teeth. Food impaction was reported more frequently in the embrasures with proximal contact loss than in those with tight contact (P=.009). Overall patient satisfaction was influenced negatively by food impaction in the proximal embrasures (P=.01). Among embrasure dimensions, only the embrasure surface area significantly influenced food impaction (P=.03). Food impaction between implant-supported FDPs and adjacent teeth occurred more frequently when proximal contact was lost and embrasure surface area increased. Food impaction also negatively affected overall patient satisfaction. Embrasure dimensions influenced the periodontal/periimplant mucosal conditions and bone level at the implant.

A similar study also examined influential factors and effects of proximal contact loss between implant-supported FDPs and adjacent teeth with additional data suggesting this problem will worsen if left untreated. In this study, 94 participants treated with 135 FDPs supported by 188 implants were included.[62] The degree of proximal contact tightness, food impaction, and periodontal/periimplant tissue conditions were assessed in 191 proximal embrasures between implant-supported FDPs and adjacent teeth. Thirty-four percent of the proximal embrasures between implant-supported FDPs and teeth lost a proximal contact. The proximal contact loss rate continuously increased over the follow-up periods. Food impaction was more frequently reported in the proximal contact loss group than in the proximal contact group with an OR of 2.2. However, in contrast with the earlier study, the proximal contact loss did not appear to affect the periodontal/periimplant tissue conditions.

The assessment of a patient's gingival and underlying bone tissue thickness is often referred to as the patient's "biotype." Treatment recommendations are frequently made based upon this characteristic. Unfortunately, objective quantification of gingival and bone tissue thickness and its correlation with an accepted biotype classifications remains elusive. Despite this, probe visibility is considered the clinical gold standard to discriminate thick from thin biotype but is prone to subjective interpretation. A study was conducted to determine at what objective gingival thickness the probe becomes invisible through the tissue.[63] A secondary objective was to compare mean buccal plate thickness between thick and thin biotypes as determined by probe visibility. Maxillary anterior teeth (n=306) were studied in 56 patients. Biotype was determined by probe visibility through the tissue. Gingival thickness was measured by transgingival sounding. Buccal plate thickness was measured (n=66 teeth) by cone beam computed tomography. For the primary objective, the gingival thickness that best corresponded with probe invisibility was selected using the receiver operating characteristic and area under the curve (AUC), with the highest combination of sensitivity and specificity. For the secondary objective, mean buccal plate thickness was compared between sites in which the probe was visible and when it was not. The gingival thickness that most closely corresponded with probe invisibility was >0.8 mm. When the probe was visible, mean gingival thickness was 0.17 mm less (P<.001) compared with the "thick" counterparts. When the probe was visible, mean buccal plate thickness tended to be smaller by 0.212 mm (P=.08), but the difference was not statistically significant. This study failed to identify a gingival thickness threshold that could discriminate reliably between sites in which the probe was visible (thin biotype) and those in which it was not (thick biotype). Probe visibility was associated with thinner measurements of gingival thickness and tended to be associated with a thinner buccal plate.

The specific advantage of administering systemic antibiotics during initial, nonsurgical therapy or in the context of periodontal surgery is unclear. A study was conducted which examined the differential outcomes of periodontal therapy supplemented with amoxicillin-metronidazole during either the nonsurgical or the surgical treatment phase.[64] A single-center, randomized placebo-controlled crossover clinical trial was conducted with a 1-year follow-up. Eighty participants with *Aggregatibacter actinomycetemcomitans*-associated moderate to advanced periodontitis were randomized into group A, consisting of antibiotics (500 mg metronidazole plus 375 mg of amoxicillin 3 times per day for 7 days) during the first, nonsurgical phase of periodontal therapy (T1) and placebo during the second, surgical phase (T2); and group B, consisting of placebo during T1 and antibiotics during T2. The number of sites with pocket depth >4 mm and bleeding on probing per patient was the primary outcome. A total of 11 212 sites were clinically monitored on 1870 teeth. T1 with antibiotics decreased the number of sites with pocket depth >4 mm and bleeding on probing per patient significantly more than without. Twenty patients treated with antibiotics but only 8 treated with placebo achieved a 10-fold reduction of

diseased sites (P=.007). Consequently, fewer patients of group A needed additional therapy, the mean number of surgical interventions was lower, and the treatment time in T2 was shorter. Six months after T2, the mean number of residual pockets was not significantly different and was sustained over 12 months in both groups. This study supports giving the antibiotics during the initial preparation phase or during the surgical phase as both yielded similar long-term outcomes. However, antibiotics in the initial preparation phase resolved the disease more quickly and thus reduced the need for additional surgical intervention.

Systemic conditions

Although prevalent periodontal disease associates with cardiovascular (CV) risk, little is known about how incident or new occurrences of periodontal disease influence future vascular risk. A large study compared the effects of incident versus prevalent periodontal disease in the development of major cardiovascular diseases (CVD), myocardial infarction (MI), ischemic stroke, and total CVD.[65] A prospective cohort of 39 863 predominantly white women ≥45 years of age and free of CVD at baseline were followed for an average of 15.7 years. Cox proportional hazard models with time-varying periodontal status, prevalent (18%), incident (7.3%) versus never (74.7%), were used to assess future CV risks. Incidence rates of all CVD outcomes were higher in women with prevalent or incident periodontal disease. For women with incident periodontal disease, risk factor-adjusted hazard ratios (HRs) were 1.42 for major CVD, 1.72 for MI, 1.41 for ischemic stroke, and 1.27 for total CVD. For women with prevalent periodontal disease, adjusted HRs were 1.14 for major CVD, 1.27 for MI, 1.12 for ischemic stroke, and 1.15 for total CVD. This study supports the fact that new diagnoses of periodontal disease, not just those which are preexisting, place women at significantly elevated risks for future CV events.

Currently, in the field of rheumatology, much attention is given to the possible causality between periodontitis and rheumatoid arthritis, specifically regarding the role of *Porphyromonas gingivalis*. This bacterium is unique, having a citrullinating enzyme. Antibodies against citrullinated proteins are rather specific for rheumatoid arthritis. Causality is ultimately tested in longitudinal cohort studies. These do not currently exist for periodontitis and rheumatoid arthritis. In a review of this systemic relationship by van de Smit et al,[66] patients with rheumatoid arthritis were found to have a higher incidence of periodontal disease than those without rheumatoid arthritis. In addition, there is a dose-response pattern in the association between the severity of periodontitis and rheumatoid arthritis disease activity. There are indications that periodontitis precedes rheumatoid arthritis, but no evidence is yet available to show that *P. gingivalis* plays a direct role in this temporal relationship. The role of the unique characteristic of citrullination by *P. gingivalis* remains unexplained. However, in animal models, citrullination by *P. gingivalis* plays a distinct role in the development and aggravation of experimental arthritis. Although the role of *P. gingivalis* in rheumatoid arthritis remains speculative, a causative role for periodontitis as a chronic inflammatory disease caused by infectious agents in rheumatoid arthritis seems biologically plausible.

Supportive data for the association of the circulating anticitrullinated protein antibody (ACPA) in patients with rheumatoid arthritis and alveolar bone loss was presented in a study by Gonzalez et al.[67] Their study examined alveolar bone loss, patients with ACPA-positive rheumatoid arthritis versus control patients with osteoarthritis, and the association of alveolar bone loss with rheumatoid arthritis disease activity and ACPA concentrations, including multiple antigen-specific ACPA. This multicenter case-control study included 617 patients diagnosed with rheumatoid arthritis (n=287) or osteoarthritis (n=330). Panoramic radiographs were made, and patients were categorized in low, moderate, or high tertiles based on mean percentage of alveolar bone loss. Serum ACPA was measured using second-generation anticyclic citrullinated peptide enzyme-linked immunosorbent assay and a multiplex platform to assess distinct antigen-specific ACPA. Associations of moderate and high alveolar bone loss (versus low) with rheumatoid arthritis disease activity and severity measurements were examined using multivariate regression. Antigen-specific ACPA responses were compared among alveolar bone loss tertiles by using significance analysis of microarrays. The authors found that patients with rheumatoid arthritis who were ACPA-positive had a significantly higher mean percentage of sites with alveolar bone loss >20% than patients with osteoarthritis. After multivariate adjustment, greater alveolar bone loss was significantly associated with higher serum ACPA concentration, 28-joint Disease Activity Score, health assessment questionnaire disability, tender joint count, and joint space narrowing scores among patients with rheumatoid arthritis. In summary, greater alveolar bone loss was associated with higher ACPA, consistent with findings at articular sites.

If rheumatoid arthritis and periodontitis present with a linked cause, the question arises whether the treatment of rheumatoid arthritis has a cross-benefit of an improvement in periodontal disease status. The benefits of anti-B lymphocyte therapy (rituximab) reducing tissue resorption in rheumatoid arthritis prompted a study to assess its potential efficacy on the periodontal status of patients with rheumatoid arthritis treated with rituximab.[68] Periodontal status was assessed in 21 participants with rheumatoid arthritis divided into 2 groups. Group I

consisted of 11 participants assessed before their first infusion of rituximab and again 6 months later. Five of them were also assessed for up to 4 years after their first rituximab infusion. The 10 participants in group II had received more than 2 courses of 2 rituximab infusions at the time of periodontal assessment. Pocket depth and AL were significantly decreased 6 months after treatment with rituximab in group I. The periodontal status of the 5 participants from group I followed for up to 48 months after rituximab treatment improved regardless of the clinical parameter observed. Patients from group II had a better periodontal status than patients from group I before treatment with rituximab. Although the sample size is small, the study suggests that anti-B lymphocyte therapy could be beneficial for improving periodontitis and suggests a role of B cells in this disease.

Periodontitis and obesity are among the most common chronic disorders, and recent reviews suggest a potential link between overweight/obesity and periodontitis. Because of the scarcity of prospective evidence, many reviews are primarily based on cross-sectional studies, with only a few longitudinal or intervention studies included. A systematic review by Keller et al[69] sought to examine the time-dependent association between obesity and periodontitis and how weight changes may affect the development of periodontitis in the general population. Intervention and longitudinal studies with overweight or obesity as exposure and periodontitis as outcome were searched through PubMed/Medline. Eight longitudinal and 5 interventional studies were included. Two of the longitudinal studies found a direct association between degree of overweight at baseline and subsequent risk of developing periodontitis, and another 3 studies found a direct association between obesity and development of periodontitis among adults. Two interventional studies of the influence of obesity on periodontal treatment effects found that the response to nonsurgical periodontal treatment was better among lean than obese patients; the remaining 3 studies did not report treatment differences between obese and lean participants. Among the 8 longitudinal studies, 1 study adjusted for C-reactive protein and biological markers of inflammation such as C-reactive protein, interleukin-6, and tumor necrosis factor-alpha, and inflammation markers were analyzed separately in 3 of the 5 interventional studies. This systematic review suggests that overweight, obesity, weight gain, and increased waist circumference may be risk factors for development of periodontitis or worsening of periodontal measures.

Approximately 1 in 8 US women (approximately 12%) will develop invasive breast cancer over the course of her lifetime. Postmenopausal survivors of this disease are often given aromatase inhibitors (AI) as part of their long-term treatment. Use of AI results in low levels of estrogen, which in turn affects bone mineral density. Periodontitis, alveolar bone loss, and tooth loss are associated with low bone mineral density. Taichman et al[70] conducted a study to assess the prevalence of periodontitis and evaluate salivary biomarkers in postmenopausal women who were survivors of early stage (I to IIIA) breast cancer (BCa) and had received adjuvant AI therapy. Participants included 58 postmenopausal women: 29 with BCa while receiving AIs and 29 controls without diagnosis of BCa. Baseline periodontal status was assessed with periodontal pocket depth, bleeding on probing, and AL. Demographic and dental use information was gathered by questionnaire. Linear regression modeling was used to analyze the outcomes. No differences were found in mean pocket depth or number of teeth. The AI group had significantly more sites with bleeding on probing (27.8 versus 16.7; P=.02), higher worst-site attachment loss (5.2 versus 4.0 mm), and more sites with dental calculus (18.2 versus 6.4) than controls. Linear regression adjusted for income, tobacco use, dental insurance, and previous radiation and chemotherapy exposure demonstrated that AI use increased attachment loss by >2 mm (95% confidence interval, 0.46 to 3.92). Median salivary osteocalcin and tumor necrosis factor-alpha levels were significantly higher in the AI group than in the control group. This is the first investigation of the periodontal status of women initiating adjuvant AI therapy which identifies this population as having an increased risk for periodontitis.

The accumulation of amyloid-beta (Abeta) plaques is a central feature of Alzheimer's disease. It remains uncertain whether peripheral inflammatory and/or infectious conditions in humans can promote Abeta brain accumulation. Periodontal disease, a common chronic infection, has been previously reported to be associated with Alzheimer's disease. Thirty-eight cognitively normal, healthy, and community-residing elderly persons (mean 61 years of age and 68% female) were examined in an Alzheimer's disease research center and a university-based dental school.[71] Linear regression models (adjusted for age, apolipoprotein E, and smoking) were used to test the hypothesis that periodontal disease assessed by clinical AL was associated with brain Abeta load using ^{11}C-labeled Pittsburgh compound B (PIB) positron emission tomography imaging. After adjusting for confounders, clinical AL ($\geq$3 mm), representing a history of periodontal inflammatory/infectious burden, was associated with increased PIB uptake in Abeta vulnerable brain regions (P=.002). This study showed for the first time in humans an association between periodontal disease and brain Abeta load.

The use of dental implants in patients receiving bisphosphonates remains controversial. A preliminary study assessed the risk of developing bisphosphonate-related osteonecrosis of the jaw in a patient with osteoporosis using zoledronic acid and reported the results

of a 1-year prospective clinical study regarding immediately inserted implants in the anterior mandible.[72] In this comparative prospective study, 24 female patients aged ≥54 years were chosen, all with partially edentulous mandibles. Group A consisted of 12 patients with osteoporosis receiving a once-yearly intravenous infusion of zoledronic acid (5 mg). Control group B consisted of 12 other patients without osteoporosis and not taking drug therapy. In both groups, the remaining teeth were extracted before 120 implants, 3.7-mm wide and 16-mm long, were immediately installed in the interforaminal regions of the mandibles. The 1-year implant survival rate was 100%. No apparent necrotic bone was observed among patients receiving zoledronic acid (group A) after implant surgery. The authors concluded that immediate implant osseointegration can be successful in a patient with osteoporosis receiving a zoledronic acid once-a-year infusion regimen.

Periodontal regeneration

Human recombinant growth factors have been shown to enhance periodontal wound healing in randomized controlled clinical trials. Kitamura et al[73] examined the efficacy, safety, and clinical significance of trafermin, a recombinant human basic fibroblast growth factor (rhFGF)-2, for periodontal regeneration in intrabony defects in Phase III trials in 2 related studies. In study A, a large multicenter, randomized, double-blind, placebo-controlled study was conducted at 24 centers. Patients with periodontitis with 4-mm and 3-mm or deeper probing pocket depth and intrabony defects, respectively, were included. A total of 328 patients were randomly assigned (2:1) to receive 0.3% rhFGF-2 or placebo, and 323 patients received the assigned investigational drug during flap surgery. One of the co-primary endpoints, the percentage of bone fill at 36 weeks after drug administration, was significantly greater in the rhFGF-2 group at 37.13% than it was in the placebo group at 21.579%. The other endpoint, the clinical attachment level regained at 36 weeks, was not significantly different between groups. In study B, a multicenter, randomized, blinded (patients and evaluators of radiographs), and active-controlled study was conducted at 15 centers to clarify the clinical significance of rhFGF-2. Patients with 6-mm or deeper probing pocket depths or 4-mm with intrabony defects were included. A total of 274 patients were randomly assigned (5:5:2) to receive rhFGF-2, EMD, or flap surgery alone. A total of 267 patients received the assigned treatment during flap surgery. The primary endpoint, linear alveolar bone growth at 36 weeks, was 1.927 mm in the rhFGF-2 group and 1.359 mm in the enamel matrix derivatives group, showing noninferiority (a prespecified margin of 0.3 mm) and superiority of rhFGF-2 to enamel matrix derivatives. Safety problems were not identified in either study. Therefore, trafermin is an effective and safe treatment for periodontal regeneration in intrabony defect, and its efficacy was superior compared with enamel matrix derivatives treatments.

In addition to the use of recombinant products, enhanced periodontal regenerative outcomes have been described using autologous growth factor preparations. One of the more commonly used preparations is platelet-rich plasma (PRP). Platelet-rich plasma is a high concentration of platelets suspended in a small volume of plasma. Although it has been broadly studied, there is much controversy as to its efficacy when used to treat intrabony periodontal defects. A systematic review and meta-analysis was conducted to assess the influence of PRP on the regeneration of periodontal intrabony defects by means of evaluating clinical and radiographic outcomes in prospective human clinical trials.[74] An electronic search of published work was conducted in several databases up to February 2014. The patient problem or population, intervention, comparison, and outcome(s) (PICO) question was does PRP have a higher efficacy for regenerating periodontal intrabony defects than or efficacy similar to other conventional periodontal regeneration treatments (such as bone grafts and barrier membranes)? Twenty-two papers were obtained and reviewed. Of these, 21 articles fulfilled the inclusion criteria and subsequently were qualitatively analyzed. Eighteen of these articles could be meta-analyzed. For pocket depth changes, the weighted mean difference (WMD) was 0.55 mm, with a 95% CI=−0.09 to 1.20 mm (P=.09). For bone level, 2 articles measured bone level in millimeters, and the other 2 articles measured bone level in percentages. The WMD was 0.76 mm and 47.41%. For attachment level changes, 12 articles were included. The WMD was 0.58 mm. Sixteen articles were included for evaluation of marginal gingival level with a WMD of −0.10 mm. High heterogeneity among studies made it difficult to draw clear conclusions. Nonetheless, within the limitations of this systematic review, PRP might have some beneficial effects on clinical and radiographic outcomes for regeneration of periodontal intrabony defects.

A similar autologous preparation is referred to as platelet-rich fibrin (PRF). Platelet-rich fibrin is considered a second-generation platelet concentrate that releases various growth factors which promote tissue regeneration in a semisolid form. Likewise, the osteoinductive property of demineralized freeze-dried bone allograft (DFDBA) has been successfully used in periodontal regeneration. A randomized controlled, split mouth clinical trial was conducted to determine the additive effects of PRF with DFDBA in the treatment of human intrabony periodontal defects.[75] Sixty interproximal infrabony defects in 30 healthy, nonsmoking patients with diagnosis of chronic periodontitis were randomly assigned to the PRF/DFDBA group or the DFDBA/saline

group. Clinical (pocket depth, clinical attachment level, and gingival recession) and radiographic (bone fill, defect resolution, and alveolar crest resorption) measurements were taken at baseline and at a 12-month evaluation. Compared with baseline, 12-month results indicated that both of the treatment modalities resulted in significant changes in all clinical and radiographic parameters. However, the PRP/DFDBA group exhibited statistically significantly greater changes than the DFDBA/saline group in pocket depth (4.15 ±0.84 versus 3.60 ±0.51 mm, respectively), clinical attachment level (3.73 ±0.74 versus 2.61 ±0.68 mm, respectively), recession (0.47 ±0.56 versus 1.00 ±0.61 mm, respectively), bone fill (3.50 ±0.67 versus 2.49 ±0.64 mm, respectively), and defect resolution (3.73 ±0.63 versus 2.75 ±0.57 mm, respectively). Observations indicate that a combination of PRF and DFDBA is more effective than DFDBA/saline for the treatment of infrabony periodontal defects.

Metformin (Glucophage), is the first-line medication for the treatment of type 2 diabetes. Metformin is also a member of the biguanide group and has been shown to facilitate osteoblast differentiation and thus may have a favorable effect on alveolar bone. A study was conducted examining the potential synergy between metformin and PRF in the treatment of periodontal defects.[76] This study was designed to evaluate the efficacy of open-flap debridement combined with PRF, 1% metformin gel, and PRF + 1% metformin gel in the treatment of intrabony defects (IBDs) in patients with chronic periodontitis. A total of 120 patients with single defects were randomized to 4 treatment groups: open-flap debridement alone, open-flap debridement with PRF, open-flap debridement with 1% metformin, and open-flap debridement with PRF plus 1% metformin. Clinical parameters such as site-specific plaque index, modified sulcus bleeding index, pocket depth, relative attachment level, and gingival marginal level were recorded at baseline (before surgery) and 9 months postoperatively. Percentage of radiographic IBD depth reduction was evaluated using computer-aided software at baseline and 9 months. The PRF, 1% metformin, and PRF plus 1% metformin groups showed significantly more pocket depth reduction and relative attachment level gain than the open-flap debridement-only group. Mean pocket depth reduction and mean relative attachment level gain were found to be greater in the PRF plus 1% metformin group compared with just PRF or metformin at 9 months. Furthermore, PRF plus 1% metformin group sites showed a significantly greater percentage of radiographic defect depth reduction (52.65% ±0.031%) than metformin (48.69% ±0.026%), PRF (48% ±0.029%), and open-flap debridement alone (9.14% ±0.04%) at 9 months. The authors concluded that the PRF plus 1% metformin group showed greater improvements in clinical parameters, with greater percentage radiographic defect depth reduction compared with metformin, PRF, or open-flap debridement alone in treatment of IBDs in patients with chronic periodontitis.

In 2014, the American Academy of Periodontology conducted systematic reviews and developed consensus statements regarding the regeneration of intrabony defects and the treatment of furcation defects. These systematic reviews and statements were published in 2015 by the American Academy of Periodontology.[77] The review focusing on periodontal regeneration approaches developed for the correction of intrabony defects considered patient-, tooth-, and site-centered factors, surgical approaches, surgical determinants, and biologics. The therapeutic endpoints examined included changes in clinical attachment level, changes in bone level/fill, and pocket depth. For purposes of analysis, change in bone fill was used as the primary outcome measurement. In all, 58 studies provided data for patient, tooth, and surgical-site considerations in the treatment of intrabony defects. A total of 45 controlled studies provided outcome analysis of the use of biologics for the treatment of intrabony defects. The evidence supports the use of biologics (enamel matrix derivatives and recombinant human platelet-derived growth factor-BB [rhPDGF-BB] plus beta-tricalcium phosphate) and demonstrates they are generally comparable with demineralized freeze-dried bone allograft and guided-tissue regeneration but superior to open flap debridement procedures in improving clinical parameters in the treatment of intrabony defects. Histologic evidence of regeneration has been demonstrated with laser therapy; however, data are limited for clinical predictability and effectiveness. This review also demonstrates that clinical outcomes appear to be most influenced by patient behaviors and the surgical approach rather than by tooth and defect characteristics. However, long-term studies indicate that improvements in clinical parameters are maintainable up to 10 years, even in severely compromised teeth, consistent with a favorable/good long-term prognosis.

The systematic review of regenerative furcation therapies presented the available evidence regarding the effectiveness of different regenerative approaches for the treatment of furcation defects in specific clinical scenarios compared with conventional surgical therapy.[78] A comprehensive search based on predetermined eligibility criteria was conducted to identify original human studies and systematic reviews of the topic of periodontal regeneration of furcation defects. The initial search yielded a total of 1500 entries. The final selection consisted of 150 articles, of which 6 were systematic reviews, 109 were clinical trials, 27 were case series, and 8 were case reports. Given the marked methodologic heterogeneity and the wide variety of materials and techniques applied in the selected clinical trials, a meta-analysis was not viable. On the basis of the reviewed evidence, the following

conclusions were drawn: (1) periodontal regeneration has been demonstrated histologically and clinically for the treatment of maxillary facial or interproximal and mandibular facial or lingual Class II furcation defects. (2) Although periodontal regeneration has been demonstrated histologically for the treatment of mandibular Class III defects, the evidence is limited to 1 case report. (3) Evidence supporting regenerative therapy in maxillary Class III furcation defects in maxillary molars is limited to clinical case reports. (4) In Class I furcation defects, regenerative therapy may be beneficial in certain clinical scenarios, although most Class I furcation defects may be successfully treated with nonregenerative therapy.

Use of lasers in periodontal therapy

Evidence has shown some limited improvement in clinical outcomes and morbidity reduction with the use of lasers for nonsurgical periodontal therapy such as ablation, vaporization, hemostasis, and field sterilization. A systematic review was conducted to evaluate and compare studies involving lasers as monotherapy or adjunctive to surgical periodontal treatment.[79] Electronic and manual searches were conducted by 2 independent reviewers in several databases. The primary outcome was pocket depth, and secondary outcomes were measured changes in clinical factors such as clinical attachment level and gingival recession. For the comparative studies included, the pooled WMD and 95% CI of each variable were calculated using random effects meta-analysis. Eight articles were included in the quantitative analyses and 9 in the qualitative analysis. Although low-to-moderate risk of bias was detected, high heterogeneity among studies was found. In flap surgery with or without laser treatment, there was no statistically significant difference in primary outcome. Similarly, in guided-tissue regeneration/enamel matrix derivatives treatment with and without laser treatment, the WMD of pocket depth was negligible; however, the guided-tissue regeneration/enamel matrix derivatives group showed better outcomes (P=.005) than the laser group. Regarding the secondary outcomes, in the flap surgery group, the WMD of clinical attachment level gain was 1.34 mm and the gingival recession WMD was −0.24 mm; no significant differences were detected between groups. In guided-tissue regeneration/enamel matrix derivatives therapy with and without laser treatment, the WMD of clinical attachment level gain was 0.10 mm, and the WMD of recession was −0.18 mm; again, no significant differences were detected between groups. The authors concluded that the available evidence is insufficient to support the effectiveness of dental lasers as an adjunct to resective or regenerative surgical periodontal therapy.

Although systematic reviews of the use of ablative laser therapy fail to demonstrate superiority over conventional therapies, investigators continue to examine the possible additive benefits of ablative laser treatment to subgingival instrumentation. A study was conducted to assess the efficacy of combining full-mouth subgingival debridement using Er:YAG laser application in the treatment of patients with chronic periodontitis.[80] In this 12-month, single-masked, parallel group clinical trial, 40 patients with moderate chronic periodontitis were selected and randomly assigned to a test group, consisting of 1 session of full-mouth ultrasonic subgingival debridement followed 1 week later by Er:YAG application in sites with initial pocket depths of ≥4.5 mm and a control group (that underwent 2 sessions of ultrasonic debridement within 1 week). The main outcome variable was change in pocket depth; the secondary outcomes were change in clinical attachment level and proportion of sites with bleeding on probing. Outcomes were assessed at baseline and after 3, 6, and 12 months. Data were analyzed as intention to treat using analysis of variance to assess intergroup differences. Both treatments resulted in significant clinical improvements. The test group achieved, in comparison with the control, a significantly lower percentage of sites with pocket depth ≥4.5 mm (17.44% versus 22.83%, respectively) and a tendency for a lower percentage of sites with pocket depth ≥4.5 mm and bleeding on probing (9.78% versus 12.69%). The authors concluded that this limited added clinical effect may justify the use of a protocol combining full-mouth ultrasonic debridement with laser therapy in the treatment of initial moderate chronic periodontitis.

Ablative laser therapy is fundamentally different from either low-level laser therapy or antimicrobial photodynamic therapy. antimicrobial photodynamic therapy is based upon the principle of eliminating cells through the use of a photosensitizing agent (optical absorption dye) and a light source (low-intensity laser with the appropriate wavelength). The goal of antimicrobial photodynamic therapy is to eliminate microorganisms present in the periodontal tissues. A randomized controlled clinical trial was conducted to evaluate the effects of repeated applications of antimicrobial photodynamic therapy adjunctive to scaling and root planing in patients with aggressive periodontitis (AgP).[81] Using a split-mouth design, 20 patients with generalized AgP were treated with antimicrobial photodynamic therapy plus scaling and root planing (test group) or scaling and root planing only (control group). Antimicrobial photodynamic therapy was applied at 4 periods. All patients were monitored for 90 days. Clinical, microbiologic, and immunologic parameters were statistically analyzed. In deep periodontal pocket analysis (pocket depth ≥7 mm at baseline), the test group presented a decrease in pocket depth and a clinical attachment gain significantly higher than that of the control group at 90 days (P<.05). The test group also demonstrated significantly less periodontal

pathogens of "red" and "orange" complexes and a lower interleukin-1beta-to-interleukin-10 ratio than the control group ($P<.05$). The authors concluded that the application of 4 sessions of antimicrobial photodynamic therapy, adjunctive to scaling and root planing, promotes additional clinical, microbiologic, and immunologic benefits in the treatment of deep periodontal pockets in single-rooted teeth in patients with AgP.

Low-level laser therapy has been shown to enhance wound healing with many tissue types, including the ability of low-level laser therapy to enhance the healing of gingival tissues after periodontal therapies. Semilunar coronally advanced flap (SCAF) and its modifications or adjuncts have been proposed in the literature for root coverage. A split-mouth randomized controlled clinical trial was conducted to assess the effects of low-level laser therapy application with respect to root coverage after SCAF procedure for the treatment of human maxillary multiple adjacent facial gingival recessions.[82] Ten participants with bilateral multiple adjacent maxillary facial gingival recession defects (Miller I and II) were included in this study (20 in test, 20 in control group). A diode laser (810 nm) at 0.3 W was applied to test sites during and 1 week after surgery for 10 seconds. Clinical measurements of surgical sites were compared. Statistically significant differences were observed between test and control sites in the change in gingival recession depth, gingival recession width, clinical attachment level, and width of the keratinized tissue measurements after 6 months. The test group presented significantly greater complete root coverage (n=18 of 20 [90%]) than with the control group (n=6 of 20 [30%]) at 6 months postoperatively. The results showed that the low-level laser technique may enhance the predictability of the SCAF procedure.

Soft tissue augmentation adjacent to teeth and implants

Recent studies have suggested that the thickness of the mucosal tissues adjacent to implants may impact the level of the crestal bone. A study was conducted to evaluate how bone-level implants maintain crestal bone stability after thickening of thin mucosal tissues with allogenic membrane.[83] A total of 97 bone-level implants of 4.1 mm diameter (Institute Straumann AG) were evaluated in 97 patients. According to vertical gingival thickness, patients were assigned into test T1 (thin, 2 mm or less, n=33), test T2 (thin thickened with allogenic membrane, n=32) and control (thick, more than 2 mm, n=32) groups. Implants were placed in the posterior mandible in a 1-stage approach, and after integration, they were restored with single-screw-retained metal ceramic restorations. Radiographic examination was performed after implant placement, 2 months after healing, after prosthetic restoration, and after 1-year follow-up. Crestal bone loss was calculated mesially and distally. After 2 months, the implants in group T1 had 0.75 ±0.11 mm bone loss mesially and 0.73 ±0.10 mm distally. Implants in group T2 had 0.16 ±0.06 mm bone loss mesially and 0.20 ±0.06 mm distally. Control group implants lost 0.17 ±0.05 mm mesially and 0.18 ±0.03 mm distally. Differences between T1 and T2 and between T1 and control were statistically significant both mesially and distally, whereas differences between T2 and control were not significant mesially and distally. After 1-year follow-up, the implants in group T1 had 1.22 ±0.08 mm bone loss mesially and 1.14 ±0.07 mm distally. Implants in group T2 had 0.24 ±0.06 mm loss mesially and 0.19 ±0.06 mm distally. Control group implants lost 0.22 ±0.06 mm mesially and 0.20 ±0.06 mm distally. Differences between T1/T2, and T1/control were statistically significant both mesially and distally, whereas between T2 and control, the differences were not significant mesially and distally. From this study, we see that significantly less bone loss can occur around bone-level implants placed in naturally thick mucosal tissues than with thin biotype. More importantly, augmentation of thin soft tissues with allogenic membrane during implant placement could be a way to reduce crestal bone loss.

A study which confirms and expands upon these findings was conducted to examine clinically and histologically the soft tissue thickening seen on acellular human dermis grafting at implant placement, taking into consideration the biotype.[84] Mucosal thickness was measured before and 4 months after implant placement when the thickness of the epithelium and corium and the inflammation were histologically evaluated with a skin biopsy. In a total of 47 implant sites (22 uncovered and 25 covered by the allograft matrix), the grafted sites showed a significantly greater increase in thickness than with the control sites. Histology was unable to show differences between groups. Nevertheless, use of an individual variation index involving the histologic and initial clinical thickness revealed that the increase in thickness of grafted sites was statistically significant compared with the decrease in control sites. Furthermore, the greatest thickness increase was recorded in sites with thin biotype, whereas a decrease was found in control sites. The inflammation index was similar in both groups. This study demonstrated the effectiveness of evaluating the increase in mucosal thickness with acellular human dermis grafting, particularly in participants with thin biotype.

Single tooth edentulous ridges present within the esthetic zone are frequently treated with either free subepithelial connective grafts or vascularized interpositional periosteal-connective tissue grafts. To test which procedure was most effective, a study was conducted to examine whether vascularized interpositional periosteal connective tissue grafts were as successful as free

subepithelial connective tissue grafts in augmenting volume defects in the anterior maxilla.[85] Twenty participants with Seibert class 1 ridge defects in the anterior maxilla were randomly and equally assigned to augmentation by vascularized interpositional periosteal connective tissue graft (test) or free subepithelial connective tissue graft (control). Clinical periodontal parameters at teeth adjacent to the gap were recorded, and conventional impressions were made before surgery and 1 month, 3 months, and 6 months after surgery. The casts were optically scanned, digitized, and analyzed for ridge contour changes in the augmented area. Significantly less shrinkage of the graft was observed in the test group after 6 months. Clinical periodontal parameters at the neighboring teeth were stable over the follow-up period and did not differ among groups. Augmentation of single tooth gaps with moderate ridge defects in the anterior maxilla was successfully performed using both techniques. However, after 6 months, sites treated by the pediculated graft were better in maintaining the initially augmented volume and showed less shrinkage of the graft. This could be attributed to better perfusion of the pediculated graft.

The use of a tunneling procedure to provide access for the placement of an acellular dermal matrix has been shown to be a highly effective method of achieving root coverage. However, further information is needed to define what clinical parameters may affect outcomes in these procedures. A study examining the influence of the location (maxilla versus mandible) and class (Miller classification) of gingival recessions on the total root coverage achievement using the tunnel procedure with acellular dermal matrix in adjacent single-root teeth was performed.[86] Twenty-four patients with 93 recessions were treated and evaluated 1 year after surgery. Results showed 100% of the root covered in 67.9% of the maxillary recessions and 52.5% in the mandible. In cases of partial root coverage, the initial recession diminished from 4.41 mm (±1.12 SD) to 0.82 mm (±0.24 SD) in the maxilla and from 3.78 mm (±1.08 SD) to 0.78 mm (±0.30 SD) in the mandible. Root coverage of 100% was observed in 74.07% of Miller Class I recessions in comparison with 43.59% of Class II recessions.

Large areas of mucogingival alterations may result from advanced regenerative procedures such as guided-bone regeneration procedures. Often the mucogingival junction is shifted toward the palatal or lingual aspect as a result of achieving primary closure during the guided-bone regeneration procedure. If the dental implants are placed in their ideal prosthetic locations, an insufficient volume of keratinized tissue often appears on the labial aspect of the implant restoration. A prospective case series study was performed to introduce and evaluate a surgical approach that combines the strip gingival graft technique with the use of a xenogeneic collagen matrix.[87] The primary outcome measurement was the increase in keratinized tissue width from baseline to 12 months after the procedure. Twenty patients were enrolled, and they all completed the 12-month evaluation. All treated sites exhibited a significant gain in keratinized tissue at 12 months, with a mean width of 6.33 mm (±2.16 SD), while there was a 43% contraction of the grafted area at 6 months. Tissue dimensions remained stable between 6 and 12 months. The use of the combination graft was well accepted by the patients, with minimal morbidity according to the patients' low self-reported pain and the low use of pain medication.

Alveolar ridge preservation and augmentation techniques

Dimensional alterations of the facial soft and bone tissues after tooth extraction in the esthetic zone play an essential role in achieving successful outcomes in implant therapy. A prospective study investigating the interplay between the soft tissue dimensions and the underlying bone anatomy during an 8-week healing period was conducted in humans.[88] The analysis was based on sequential 3-dimensional (3D) digital surface model superimpositions of the soft and bone tissues using digital impressions and cone beam computed tomography during an 8-week healing period. Soft tissue thickness in thin and thick bone phenotypes at extraction was similar, averaging 0.7 mm and 0.8 mm, respectively. Interestingly, thin bone phenotypes revealed a 7-fold increase in soft tissue thickness after an 8-week healing period, whereas in thick-bone phenotypes, the soft tissue dimensions remained unchanged. The observed spontaneous soft tissue thickening in thin-bone phenotypes resulted in a vertical soft tissue loss of only 1.6 mm, which concealed the underlying vertical bone resorption of 7.5 mm. Because of spontaneous soft tissue thickening, no significant differences were detected in the total tissue loss between thin and thick bone phenotypes at 2, 4, 6, and 8 weeks. More than 51% of these dimensional alterations occurred within 2 weeks of healing. These findings are significant as they demonstrate that bone volumes are not reflective of the overlying soft tissue profiles in a healing extraction site. Even though the observed spontaneous soft tissue thickening in thin-bone phenotypes after tooth extraction conceals the pronounced underlying bone resorption pattern by masking the true bone deficiency, spontaneous soft tissue thickening offers advantages for subsequent bone regeneration and implant therapies in sites with high esthetic demand.

As platelet concentrates have been shown to be of benefit in the healing of periodontal defects, a systematic review was undertaken to evaluate the effect of autologous plasma concentrates on the preservation of the alveolar bone and soft tissue associated with extraction sockets.[89] A comprehensive literature search was

performed in the MEDLINE/PubMed and Cochrane Central Register of Controlled Trials (CENTRAL) databases. Four studies, published between 2010 and 2013, met the eligibility criteria and were included in the review. There were 102 extractions (55 tests, 47 controls) in 82 patients. Considerable heterogeneity existed between studies with regard to the design, follow-up time, surgical techniques, and method of preparation of plasma concentrates, and therefore the data could not be analyzed quantitatively. The authors concluded that the use of plasma concentrates seems to accelerate healing and soft tissue epithelialization in extraction sockets and reduce postoperative pain and discomfort. However, there is no evidence to date to confirm that plasma concentrates improve hard tissue regeneration.

A study was conducted to evaluate the effect of mineralized freeze-dried bone allograft (FDBA), alone or in combination with growth factors in extraction sockets, on the subjective assessment of bone quality during implant placement.[90] Forty-one patients whose treatment plan involved extraction of anterior or premolar teeth were randomized into 4 groups: group 1 received a collagen plug (control); group 2 received an FDBA/beta-tricalcium phosphate (beta-TCP)/collagen plug; group 3 received an FDBA/beta-TCP/PRP/collagen plug; and group 4 received an FDBA/beta-TCP/rhPDGF-BB)/collagen plug. After 8 weeks of healing, implants were placed. The clinicians assessed bone quality according to the Misch classification which define 4 bone density classes (D1-D4) based on the clinical drilling resistance of the bone. A benchtop calibration exercise test was conducted to evaluate the agreement and accuracy of operators in recognizing different bone qualities. The benchtop calibration exercise test demonstrated agreement among clinicians (0.75 between raters 1 and 2 and 0.92 between raters 1 and 3). Raters were more likely to identify the correct bone quality ($P>.05$). Inclusion of bone grafting is associated with a shift from D4 quality to D3 quality bone. Inclusion of PRP in bone grafting eliminates the incidence of D4 bone, establishing D3 and D2 quality bone as prevalent (56% versus 42%, respectively). Inclusion of rhPDGF-BB and beta-TCP in combination with the bone grafting has the same effect, although D2 quality is less prevalent. Compared with sockets grafted with FDBA/beta-TCP/collagen plug alone, the sockets with growth factors demonstrated fewer residual bone graft particles. The authors concluded that the inclusion of bone grafting enhanced bone quality as assessed during implant placement. Also the overall inclusion of PRP and rhPDGF-BB enhanced subjective bone quality, eliminating the incidence of D4 quality in human extraction sockets.

Lateral ridge augmentation procedures are aimed at reconstructing deficient alveolar ridges or repairing periimplant dehiscence and fenestrations. A systematic review was performed to assess the efficacy of these interventions by analyzing data from 40 clinical studies which evaluated bone augmentation through either the staged or the simultaneous approach.[91] The primary outcomes were the changes at reentry, in the ridge width, and in the vertical and horizontal dimensions of the periimplant defect, measured in millimeters, in the staged and simultaneous approaches, respectively. The results of the meta-analysis showed, for the simultaneous approach, a statistically significant reduction in defect height when all treatments were analyzed together (WMD =−4.28 mm. The intervention combining bone replacement grafts with barrier membranes was associated with better outcomes. The most frequently used intervention was the combination of xenograft and bioabsorbable membrane. Similarly, for the staged approach, a statistically significant horizontal gain was noted when all treatment groups were combined WMD=3.90. The most frequently used intervention was the use of autogenous bone blocks. Both of the treatment strategies led to high survival and success rates (>95%) for the implants placed on the regenerated sites.

Guidelines regarding the ideal time to place implants in augmented sinus cavities are often not empirically based. An investigation was made to examine the amount of mineralization of a bovine bone substitute material in sinus floor augmentation after healing times of 3 and 6 months.[92] A cohort of 51 patients were randomized into 2 healing time groups and received sinus floor augmentations with a bovine bone material. After 3 or 6 months of healing, trephine bone biopsies were performed. The biopsy samples were processed for histological and histomorphometric evaluations to primarily investigate the amount of mineralized bone in the augmented area and secondarily to compare the amount of mineralized bone in the augmented area and in the pristine bone. The analysis of biopsies of both groups showed remnants of the well-integrated bone substitute material. The histology revealed osteoblasts, osteocytes with osteoid, and osteoclasts. The mean percentage of mineralized bone in the augmented area was 23.8% (3 months group) and 23.6% (6 months group; $P=.9246$); the amount of remaining bone substitute material was 35% (3 months group) and 33.9% (6 months group; $P=.6325$). The authors concluded that the bone maturation in the augmented sinus using the bovine bone material was similar after 3 and 6 months. The authors stated that implant installation 3 months after a lateral window sinus floor augmentation approach with a bovine bone material seems to be clinically acceptable. Studies examining the long-term survival of implant prostheses loaded at these time intervals are required to support these claims.

Periimplantitis

A systematic review examining the existing evidence for identifying risk indicators in the cause of periimplantitis was published.[93] The literature search was performed in

MEDLINE for articles published until October 2014. This review found that the microbiota associated with periimplantitis is complex, demonstrating differences and similarities to that seen at periodontitis sites. Plaque accumulation at dental implants triggers the inflammatory response leading to periimplant mucositis/periimplantitis. Individuals with a history of periodontal disease and smokers have an increased risk of developing periimplantitis. There is some evidence to support the role of genetic polymorphism, diabetes, and excess cement as risk indicators for the development of periimplantitis. There is also evidence to support that individuals on regular maintenance are less likely to develop periimplantitis and that successful treatment of periodontitis prior to implant placement lowers the risk of periimplantitis. The authors concluded that plaque accumulation at implants will result in the development of inflammation. A history of periodontal disease, smoking, excess cement, and lack of supportive therapy should be considered as risk indicators for the development of periimplantitis.

Excess cement left in the periimplant sulcus after the placement of prosthetic restorations risks inflammation in the periimplant tissue. Although many current studies deal with the question of how to avoid undetected excess cement, relatively little is known about the clinical consequences of this complication. Korsch et al[94] conducted a study analyzing the clinical findings associated with excess cement. Furthermore, the influence of the sojourn time of undetected excess cement in the periimplant pocket on clinical findings was investigated. Within the scope of this retrospective clinical follow-up, the suprastructures that were originally cemented with a methacrylate cement were revised in 93 patients (171 implants). The patients were split into 2 groups according to the time between placement of the prosthetic restoration and revision. Group 1 had treatment revisions within 2 years of restoration placement (71 patients with 126 implants); in group 2, treatment revisions were conducted at a later time (22 patients with 45 implants). For the purpose of statistical analysis, both of the groups were further analyzed based on the presence/absence of excess cement at the time of revision. By definition, the average time to revision in group 1 was shorter than in group 2 (0.71 years versus 4.07 years). No significant difference was found in the frequency of excess cement at revision between group 1 (59.5%) and group 2 (62.2%). The clinical findings around the implants in group 1 were significantly less severe than those in group 2. After excess cement was removed, and implant abutment was cleaned and disinfected and restored, and using a different cement, significantly fewer signs of inflammation were found at further follow-up in both groups. Within the limitations of this retrospective observational study, excess cement was present in a high number of cement-retained implant restorations. Signs of inflammation were present in a large proportion of implants at short- to medium-term follow-up. At the time of restoration revisions, the clinical observation of previously undetected excess cement was associated with an increased prevalence of inflammation. Removal of excess cement significantly reduced the signs of inflammation.

To evaluate the prevalence of periimplant diseases and to analyze possible risk variables associated with their occurrence, a study was done in 186 patients with 597 implants who were examined clinically and radiographically.[95] The mean period of function was 5.5 years (range: 1-16.5 years). A subgroup analysis was performed for implants with a minimum function time of 5 years. Outcome measures were implant failures, prevalence, and risk indicators of periimplant diseases. In order to identify statistically significant risk indicators of periimplant mucositis and periimplantitis, multilevel logistic regression models were constructed. The prevalence of periimplantitis and periimplant mucositis at the patient level was 12.9% (13.3% for $\geq$5 years) and 64.5% (64.4% for $\geq$5 years), respectively. Multilevel analysis showed that a high plaque score was a risk indicator for periimplant mucositis, while augmentation of the hard or soft tissue at implant sites had a protective effect. Also, the odds ratio for having periimplant mucositis increased with the increase of plaque score in a dose-dependent manner. With respect to periimplantitis, the loss of the last tooth because of periodontitis and the location of the implants in the maxilla were identified as statistically significant risk indicators. Within the limitations of this study, the history of periodontal disease was the most significant risk indicator for periimplantitis, and the level of oral hygiene was significantly associated with periimplant mucositis.

Smokers are at high risk for 2 bacterially driven oral diseases: periimplant mucositis and periimplantitis. An investigation was conducted to examine the use a deep-sequencing approach to identify the effect of smoking on the periimplant microbiome in states of health and disease.[96] Periimplant biofilm samples were collected from 80 partially edentulous participants with periimplant health, periimplant mucositis, and periimplantitis. Bacterial DNA was isolated and 16S ribosomal RNA gene libraries were sequenced using 454-pyrosequencing targeting the V1 to V3 and V7 to V9 regions. In total, 790 692 classifiable sequences were compared against the Human Oral Microbiome Database (HOMD) database for bacterial identification. Community-level comparisons were carried out using UniFrac method and nonparametric tests. UniFrac is a new phylogenetic method that measures the distance between communities based on the lineages they contain. Microbial signatures of health in smokers exhibited lower diversity compared with nonsmokers, with significant enrichment for disease-associated species. Shifts from health to

mucositis were accompanied by loss of several health-associated species, leading to a further decrease in diversity. Periimplantitis did not differ significantly from mucositis in species richness or evenness. In nonsmokers, by contrast, the shift from health to mucositis resembled primary ecological succession, with acquisition of several species without replacement of pioneer organisms, thereby creating a significant increase in diversity. Again, few differences were detected between periimplantitis and mucositis. These data suggest that smoking shapes the periimplant microbiomes, even in states of clinical health, by supporting a pathogen-rich community. In both smokers and nonsmokers, periimplant mucositis appears to be a pivotal event in disease progression, creating high at-risk-for-harm communities.

Long-term studies worldwide indicate that periimplant inflammation is a frequent finding and that the prevalence of periimplantitis correlates with loading time. Implant loss, although less frequent, has serious oral health and economic consequences. An understanding of predictive factors for periimplant disease and implant loss would help providers and patients make informed decisions. To better define these predictive factors, a cross-sectional study was performed on 96 patients with 225 implants that were placed between 1998 and 2003.[97] Implant placement data were collected from patient records, and patients presented for a clinical and radiographic follow-up examination. Implant status and periodontal status were determined, the data were analyzed to determine the prevalence of periimplant disease or implant loss, and a predictive model was tested. The mean follow-up time for the patients was 10.9 years. The implant survival rate was 91.6%. Periimplant mucositis was found in 33% of the implants and 48% of the patients, and periimplantitis occurred in 16% of the implants and 26% of the patients. Individuals with periimplantitis were twice as likely to report a problem with an implant compared with individuals with healthy implants. Periimplantitis is associated with younger ages and diabetes at the time of placement and with periodontal status at the time of follow-up. Implant loss is associated with diabetes, immediate placement, and larger-diameter implants. The authors concluded that one in four patients and one in six implants have periimplantitis after 11 years. The data suggest that the periodontal and diabetic status of the patient may be useful for predicting implant outcomes and the rate of prevalence periimplantitis should be shared with patients considering implant therapies.

As abundant evidence supports an association between the microbiome and periimplantitis, the physical location of the bacteria as it relates to the implant and the restorative interface is a factor of interest. Canullo et al[98] compared implants under healthy conditions and implants with periimplantitis with regard to their clinical parameters and the microbiologic composition at the periimplant sulcus, inside the implant connection, and at the gingival sulcus of neighboring teeth. A cross-sectional study was performed with consecutive patients with implants in healthy conditions and with periimplantitis. Clinical parameters for which patients were screened included bleeding on probing, pocket depth, and plaque index at 6 sites. Specimens for microbiologic analysis were obtained from 3 locations: the periimplant sulcus, inside the implant connection, and the gingival sulcus of neighboring teeth. Quantitative real-time polymerase chain reaction (PCR) was carried out for total counts of 10 microorganisms. The response variables were the percentage of positive sites and total bacterial counts. A total of 122 implants in 57 patients were analyzed in the healthy group and 113 implants in 53 patients in the periimplantitis group. Differences between the groups were statistically significant for bruxism, probing pocket depth, bleeding on probing, and radiographic bone level. Orange complex species (*Prevotella intermedia*, *Peptostreptococcus micros*, *Fusobacterium nucleatum*) were the most prevalent in the 3 types of sites for both groups, and prevalence values were higher in the periimplantitis group. Differences in prevalence between groups were more marked inside the connection than in the periimplant sulcus. Absolute loads of most microbes and total bacterial counts were higher for the periimplantitis group in the 3 locations. Again, differences were bigger inside the connection than at the periimplant sulcus. Significant interactions were found for prevalence and absolute microbial loads between groups and locations. Microbiologic differences between groups were more marked inside the connection than in the periimplant sulcus. The authors suggested that the potential role of the implant connection as a microbial reservoir for periimplant diseases and in the outcome of their treatment should be confirmed with further studies.

It is now commonly understood that periimplantitis is an inflammatory condition that can lead to implant loss. What is unknown is whether the microbiologic changes are causative or associative. Wilson et al[99] undertook a descriptive retrospective study, examining the histopathologic findings in soft tissue biopsies of implants with periimplantitis. The 36 human periimplantitis biopsies were analyzed using light microscopy and scanning electron microscopy (SEM). The composition of foreign materials found in the tissues was assessed using an energy dispersive x-ray spectrometer. At the light microscopy level, the inflammatory lesion of periimplantitis was in most cases a mixture of subacute and chronic inflammation dominated by plasma cells. At the SEM level, radiopaque foreign bodies were identified in 34 of the 36 biopsies. The predominant foreign bodies found were titanium and dental cement. These foreign materials were surrounded by inflammatory cells. At

present, the exact mechanism for the introduction of these materials and their role in periimplantitis is unknown. Further research is warranted to determine their cause and potential role in pathogenesis. This study may be significant in our understanding of the cause of periimplantitis. These fragments of "foreign body" materials in the surrounding periimplant soft tissues may support the theory that periimplantitis occurs as a result of foreign body reaction to either the implant, the prosthetic materials, or both.

Albrektsson et al[100] discussed the concept of a "disbalanced" foreign body reaction as the cause of early marginal bone loss. When a foreign body is placed in bone or soft tissue, an inflammatory reaction inevitably develops. Hence, osseointegration is but a foreign body response to the implant, which according to classic pathology is a chronic inflammatory response and characterized by bone embedding/separation of the implant from the body. The authors suggested an alternative way of looking at the reason for marginal bone loss as a complication to treatment rather than a disease process. They suggested that the implant-enveloping bone has sparse blood circulation and is lacking proper innervation in clear contrast to natural teeth that are anchored in bone by a periodontal ligament rich in blood vessels and nerves. Fortunately, a balanced, steady-state situation of the inevitable foreign body response will be established for the great majority of implants, seen as maintained osseointegration with no or only very little marginal bone loss. The authors go on to suggest that marginal bone resorption around the implant is the result of different tissue reactions coupled to the foreign body response and is not primarily related to biofilm-mediated infectious processes as in the pathogenesis of periodontitis around teeth. This means that initial marginal bone resorption around implants represents a reaction to treatment and is not at all a disease process. There is clear evidence that the initial foreign body response to the implant can be sustained and aggravated by various factors related to implant hardware, patient characteristics, surgical and/or prosthodontic mishaps, which may lead to significant marginal bone loss and possibly to implant failure. The authors go on to suggest that once severe marginal bone loss has developed, a secondary biofilm-mediated infection may follow as a complication to the already established bone loss.

The ideal treatment for periimplantitis remains elusive. Some treatments have focused on the use of lasers to decontaminate the implant surface. A systematic review was conducted to evaluate the efficacy of various types of lasers (Nd:YAG, CO_2, diode Er,Cr:YSGG, and Er:YAG) in the treatment of periimplantitis and their use in surgical and nonsurgical procedures.[101] Human studies for the treatment of periimplantitis with laser therapy, published between 2002 and January 2014, were collected from the electronic databases. A total of 812 studies were selected in the initial title search; 13 studies were then chosen for this review. No human studies evaluated the effect of the Nd:YAG laser on periimplantitis. The CO_2 laser is reported to be safe and able to enhance bone regeneration. The diode laser (980 nm) seems to be effective in its bactericidal effect without changing the implant surface pattern. The Er, Cr:YSGG laser was reported to obtain bone regeneration around a failing implant in one case, whereas the Er:YAG laser exhibits a strong bactericidal effect against periodontopathic bacteria at a low energy level. Although lasers have shown promising results in reducing clinical signs of periimplantitis, because of the limited sample sizes and short follow-up periods, no firm conclusion can be drawn at this moment.

PROSTHODONTICS

The section on prosthodontics is divided into 8 convenient subtopics: (1) general prosthodontic considerations, (2) conventional removable complete prosthodontics, (3) conventional removable partial prosthodontics, (4) conventional fixed prosthodontics, (5) general implant prosthodontic considerations, (6) implant removable prosthodontics, (7) implant fixed prosthodontics, and (8) prosthodontic materials. Several excellent general and systematic reviews published on topics of prosthodontic interest appeared in the 2015 literature, as follows: fixed prosthodontics,[102-105] removable prosthodontics,[106-109] occlusion,[110-114] prosthodontic materials,[115-123] bruxism and tooth structure loss,[124-129] treatment planning,[130-135] cancer patient management,[136-146] xerostomia,[147-149] the medically compromised patient,[150-154] medication-related osteonecrosis of the jaw,[155-162] digital dentistry,[163,164] accidental swallowing,[165,166] pharmacology,[167-170] and evidence-based dentistry.[171]

General prosthodontic considerations

As the current gold standard for measuring therapeutic effectiveness, randomized controlled clinical trials (RCTs) are susceptible to various forms of bias, including selection, performance, detection, attrition, and reporting biases. In a cross-sectional study, Papageorgiou et al[172] assessed the risk of bias in RCTs recently published in prosthodontic and implant dentistry journals. Relevant articles were extracted from the last 30 issues of 9 major journals in the target fields. Internal validity was assessed using the Cochrane Collaboration's risk of bias tool and analyzed using descriptive statistics. Specifically, this tool examined 7 domains, including random sequence generation, allocation concealment, masking (blinding of participants and personnel), blinding of outcome assessment, incomplete outcome data, reporting bias, and other bias sources.

Of the 3667 articles screened, 147 RCTs met inclusion criteria. For the included RCTs, a high risk of bias was found in 8% for random sequence generation, 18% for allocation concealment, 41% for masking, 47% for blinding of outcome assessment, 7% for incomplete outcome data, 12% for selective reporting, and 41% for other biases.

The authors concluded that the distribution of a high risk of bias for RCTs published in the selected prosthodontic and implant dentistry journals varied among journals and ranged from 8% to 47% in the various domains examined, which is of considerable concern. Closer adherence to published guidelines for the conduct of RCTs may facilitate improved trial and reporting quality.

Conventional removable complete denture prosthodontics

Pneumonia represents a significant health risk among elderly individuals. Aspiration is a significant pathogenic mechanism for pneumonia that may be reduced by competent professional oral care, particularly among medically compromised elderly individuals. Iinuma et al[173] prospectively examined associations between oral health behaviors (risk factors) and pneumonia events in very elderly community-living individuals. The authors sought to identify modifiable oral health-related risk factors that could provide tangible benefits in pneumonia prevention.

The study populations consisted of 524 randomly selected Japanese seniors (mean of 87.8 years of age, range of 85 to 102 years; 228 men, 296 women). The participants were examined for oral health status, oral health behaviors, oral health quality of life, and ability to eat 15 different food items. For those wearing dentures, information on denture hygiene practices and frequency/duration of daily denture wear was gathered. Medical assessments included physical examination, cognitive assessment, pharmacologic registration, and blood chemistry analysis. Follow-up surveys were conducted annually. Those remaining in the cohort at 3 years were reexamined according to the initial protocol. The patients were followed for up to 3 years, or until first pneumonia-related hospitalization or pneumonia-related death.

During follow-up, 48 pneumonia-related events occurred (20 deaths, 28 acute hospitalizations) for an annual incidence of serious pneumonia of 3.1 per 100. Among 453 denture wearers, 186 (40.8%) those wearing dentures during sleep were at higher risk for pneumonia than those who removed dentures at night (P=.021). Statistically, both perceived swallowing difficulties and overnight denture wear were independently associated with an approximately 2.3-fold higher risk of the incidence of pneumonia (comparable to cognitive impairment, history of stroke, and respiratory disease). Wearing dentures at night was found to be associated with poor denture hygiene practices, fewer dental office visits, denture and tongue plaque, gingival inflammation, oral candidiasis, and higher levels of circulating interleukin-6, suggesting that nighttime denture wear could be a sensitive marker identifying those at high risk of both poor oral health and aspiration pneumonia.

The authors conclude that the empirical evidence associates wearing of dentures during sleep with adverse oral conditions, microbial complications, and incident pneumonia, all life-threatening complications in very elderly community-living individuals. Determining biological mechanisms by which denture wearing during sleep precipitates these risks may lead to effective preventive interventions in denture wearing patient populations.

Malnutrition is a substantial geriatric concern affecting a significant percentage of nursing home residents. However, the current literature lacks evidence of the relationship between dental status and malnutrition in this at-risk population. Therefore, Zenthofer et al[174] examined associations between prosthodontic status and malnutrition in institutionalized elders. A total of 255 residents (mean of 83.2 years of age; 79 males, 176 females) from 14 nursing homes were examined to assess dental status, denture quality (fit and retention), nutritional status (body mass index [BMI] and care dependency (Barthel index). Of those participants who wore dentures of any kind (n=186), 101 were edentulous.

Based on BMI, the study population consisted of 33 malnourished and 222 adequately nourished participants. The number of natural teeth and prevalence of adequate prosthodontic rehabilitation were significantly lower in malnourished individuals (P<.05). Logistic regression modeling for all participants revealed a 4.6-fold greater risk of malnutrition for edentulous individuals not wearing dentures. Logistic regression modeling for denture wearers indicated that denture fit and retention were not predictors of malnutrition.

The authors concluded that inadequate prosthodontic tooth replacement, including unrestored edentulism, is associated with substantially greater risk of malnutrition in institutionalized elders. The impact of lack of nutrition linked to ill-fitting, nonretentive complete dentures may indicate effective use of adhesives and/or successful adaptation to poorly fitting dentures. The results suggest that adequate prosthodontic tooth replacement supports adequate nutrition in this needy institutionalized population.

Currently, most dental schools advocate making 2 impressions during conventional complete denture fabrication; a stock tray irreversible hydrocolloid primary impression and a border molded custom tray silicone-based definitive impression. However, current research

indicates the use of a single irreversible hydrocolloid impression by many general practitioners in the private sector. Jo et al[175] conducted a randomized crossover controlled clinical trial assessing the efficiency of the conventional method (2 impressions) compared with a simplified method (single impression) during definitive complete denture fabrication.

Twenty-four patients with edentulism (mean of 74 years of age; 11 men, 13 women) requiring complete dentures entered the trial. The prostheses were fabricated using identical processes, except for definitive mandibular impression methods. The conventional method involved an impression plastic border molded custom tray washed with silicone impression material. The simplified method used an edentulous metal stock tray and irreversible hydrocolloid impression material. Each participant received mandibular complete dentures fabricated from impression methods. The participants were randomly allocated to 1 of 2 groups: a conventional-simplified group (wore conventional method complete denture first, followed by the simplified) and a simplified-conventional group (wore simplified method complete denture first, followed by conventional). A washout period of 1 month was used. The participants rated general satisfaction (primary outcome) with new complete dentures using a visual analog scale. Oral health-related quality of life (secondary outcome) was measured using the Japanese version of the Oral Health Impact Profile for patients with edentulism (OHIP-EDENT-J) questionnaire scores. OHIP-EDENT-J is a questionnaire on oral health quality of life consisting of 19 items.

Based on general satisfaction, the conventional mandibular impression method produced complete dentures rated significantly more acceptable by patients than the simplified method. No significant differences were observed between the 2 methods based on health-related quality of life measures, possibly influenced by the limitations of short-term data collection.

Although the crossover study design prohibited long-term data collection, the authors concluded that patients preferred mandibular complete dentures fabricated using a conventional 2-impression method. It was suggested that future studies should focus on cost-effectiveness when comparing the conventional and simplified methods for the complete denture fabrication.

An increasing elderly patient population has impacted, and will continue to impact, demands on the profession for high-quality complete denture service. Because patient satisfaction is a desirable outcome in complete denture therapy, a thorough understanding of the multifactorial nature of this parameter is imperative. Santos et al[176] evaluated patient expectations before and patient satisfaction after therapy to provide conventional complete dentures. Other variables that may interfere with patient satisfaction were also assessed.

A representative sample of 99 patients with edentulism (mean 53 years of age; age range: 32 to 81 years of age; 61 men, 38 women) participated. Pretreatment patient expectations and posttreatment satisfaction (based on mastication, esthetics, comfort, and phonetics) were assessed using visual analog scales (VAS). Patient demographics (sex, age, education, marital status, denture experience, and adjustments needed after delivery) were collected. The patient's opinions of provider conduct were assessment via questionnaire. Associations among all variables and expectations/satisfaction were determined using multiple linear regression.

The results demonstrated that average VAS scores were high for both patient expectations and satisfaction, with patient satisfaction exceeding expectations. Patient esthetic and comfort expectations were associated with age and denture experience. Mastication satisfaction was associated with the number of adjustments after delivery. Esthetic satisfaction was associated with sex and esthetic expectations. Patient phonetic satisfaction was associated with denture experience, comfort expectations, phonetics expectations, and dentist's explanations. Comfort satisfaction was associated with educational level.

The authors concluded that, in the population investigated, patient satisfaction with new complete dentures exceeded their pretreatment expectations. Many pretreatment and post-treatment patient-related variables seemed to influence evaluations of newly provided complete dentures. Additionally, patients receiving pretreatment therapeutic explanations from dentists appeared more satisfied with treatment results, suggesting the patient/provider relationship is a key factor in successful complete denture therapy. Unfortunately, the use of a quantitative approach and statistical association-based analyses limited the assignment of cause-effect relationships among the variables assessed.

Conventional removable partial prosthodontics

The crown-root ratio (CRR) is a common objective clinical index typically used to assess expected stability and durability of prosthodontic abutments. Although appropriate CRRs have been suggested historically, there appears to be no universally accepted threshold ratio because of a lack of longitudinal clinical data associating CRR and abutment survival. Therefore, Tada et al[177] conducted a longitudinal (up to 7 years) practice-based study assessing the impact of CRR on the survival of abutments for removable partial dentures (RPDs).

Data were collected from 147 patients (mean 64 years of age; 55 men, 92 women) provided with RPDs at a dental hospital in Japan. In total, 236 clasp-retained RPDs and 856 abutments were analyzed. According to the Kennedy classification, 99 RPDs were class 1, 99 were class 2, and 38 were class 3 or 4. On average, the RPDs examined remained in service approximately 5.5 years,

replaced 5.3 missing teeth, and were supported by 3.7 abutments. The CRR was measured on radiographs made at the time of RPD placement. Abutments were divided into 1 of 5 risk groups A to E according to baseline CRR, where A represented <0.75; B, 0.76-1.00; C, 1.01-1.25; D, 1.26-1.50; and E, >1.51. Kaplan-Meier methods qualified abutment survival. The Cox proportional hazards regression was used to assess prognostic significance of initial CRRs adjusted for clinically relevant factors (age, sex, periodontal maintenance frequency, occlusal support area, type of abutment, endodontic treatment status, and pocket depth).

The results indicated a 7-year survival rate for groups as follows: A=89.1%; B=85.9%; C=86.5%; D=76.9%; and E=46.7%. The survival curves of groups A, B, and C were determined to be similar and more favorable than those for groups D and E. Multivariate analysis treating CRR as a continuous variable allowed estimation of the HR (HR or risk of tooth loss) at any specific CRR value. Estimated HRs (withe CRR=0.80 reference) were as follows: 0.58 for CRR=0.50, 1.13 for CRR=1.00, 1.35 for CRR=1.25, 1.53 for CRR=1.50, and 1.95 for CRR=2.00.

The authors concluded that this practice-based longitudinal study demonstrated the impact of CRR on the survival of RPD abutments. Data suggested that groups A, B, and C (CRR$\leq$1.25) were similar, with outcomes preferred to those of groups D and E. Groups D and E (CRR$\geq$1.26) had poor survival rates. The authors added that this longitudinal practice-based cohort study confirmed that a higher CRR was associated with greater risk of RPD abutment loss. Moreover, the specific risk of abutment loss relative to CRR can be estimated after adjusting other variables. The authors stressed that results presented here can help guide clinical decisions related to using teeth with compromised periodontal support as abutments for removable prostheses.

Intuitively, the primary goal of prosthodontic rehabilitations with RPDs is replacement of missing teeth to restore impaired masticatory function. In considering Kennedy class 1 partial edentulism, the need to provide prosthetic replacement for missing posterior teeth has been questioned. An evidentiary basis for providing extension base RPDs to improve masticatory performance in patients with shortened dental arches (shortened dental arches, 3 to 5 posterior occluding pairs) or extreme shortened dental arches (extreme shortened dental arches, 0 to 2 posterior occluding pairs) is unclear. Although publications addressing this clinical question exist, varied methodologies and materials for assessing masticatory performance render it difficult to appraise outcomes comprehensively. Liang et al[178] systematically reviewed available dental literature to synthesize existing knowledge on the effects of distal extension RDPs on the masticatory performance of patients with shortened dental arches or extreme shortened dental arches.

An electronic search was conducted using readily available databases. Studies addressing shortened dental arches/extreme shortened dental arches and masticatory performance with RPDs were included. Initially, this strategy yielded 1210 articles. Following review and application of inclusion/exclusion criteria, 8 articles were identified and entered the systematic review: 4 studies reported on comminution (particulation) of test food, 3 on mixing of test food, and 1 incorporating both tests.

The results indicated a significant relationship between number of artificial teeth in experimental distal extension RPDs for participants with extreme shortened dental arches and masticatory performance. Comminution or mixing ability in participants with unrestored extreme shortened dental arches was 28% to 39% lower than participants with complete dentitions. Two studies demonstrated improved comminution when masticating with an RPD than without the RPD. One study reported 28% to 83% lower mixing ability when chewing on the RPD side than the dentate side. Generally, more artificial teeth (or longer prosthetic occlusal platform) in experimental RPDs resulted in better comminution and better mixing ability, which was significant in 4 out of 5 studies.

The authors concluded that extension-based RPDs seem to offer limited improvements in objective mastication function for patients with extreme shortened dental arches. However, considering cost-effectiveness, the use of an RPD to extend the shortened dental arches to improve masticatory performance may not be indicated. Participants with extreme shortened dental arches demonstrate a 30% to 40% reduced masticatory performance with partial compensation provided by extension base RPDs. For patients with extreme shortened dental arches, the greater the number of prosthetic teeth, the better the masticatory performance. Generally, extension base RPDs in patients with extreme shortened dental arches appear to partially compensate for reduced masticatory performance resulting from missing posterior dentition.

As historically proposed, a patient with a shortened dental arch (shortened dental arches) with at least 4 posterior occluding units is thought to possess sufficient adaptive capacity to maintain adequate oral function. While this concept is widely accepted in European countries as an alternative to prosthodontic treatment of partial edentulism, practical application of the shortened dental arches concepts is debated in Japan and other regions of the world. To address the validity of shortened dental arches relative to oral health-related quality of life (OHRQoL), Fueki et al[179] published a multicenter prospective study investigating the effect of prosthodontic replacement of missing posterior teeth in patients with shortened dental arches.

Patients with 2 to 12 missing occlusal units (1 pair of occluding premolars=1 occlusal unit; 1 pair of occluding molars=2 occlusal units) were consecutively enrolled from 7 university-based dental hospitals. Patients were permitted to choose 1 of 3 treatment options: no replacement of missing teeth, RPDs, or implant-supported fixed partial dentures (IFPDs). The oral health impact profile (Japanese version, OHIP-J) was used to measure OHRQoL at baseline and post-treatment evaluations. Of the 169 participants who completed baseline evaluation, 125 participants (mean 63 years of age) were evaluated at all 3 post-treatment intervals.

Of the 125 participants, 42% (n=53) chose no treatment, 42% (n=53) chose an RPD, and 16% (n=19) elected IFPDs. In the no-treatment group, the mean OHIP summary score at baseline was similar to that at follow-up evaluation (P=.69). In the treatment groups, the mean OHIP summary score decreased (improved) significantly after RPD treatment (P=.002), and it tended to decrease, although not significantly (P=.18), following IFPD treatment. Regression analysis indicated that the replacement of 1 occlusal unit was associated with a 1.2-point improvement in OHIP summary score (P=.034), suggesting that the number of replaced occlusal units was positively associated with OHRQoL.

The authors were quick to indicate study limitations: the allocation of patients was not random for obvious ethical reasons; sample size (particularly for the IFPD group) was small, potentially making OHIP comparisons suspect; impact of treatment effects on OHRQoL may be more substantial over greater follow-up periods; and presenting oral conditions and patient prosthodontic experiences may have influenced results. The authors concluded that, within study limitations, the prosthodontic replacement of missing posterior teeth in shortened dental arches patients using RPDs and IFPDs appeared to benefit OHRQoL.

It is generally considered desirable to extend mandibular RPD extension base borders to cover some or all of the retromolar pads. The rationale for this clinical objective relates primarily to 2 theories: broad coverage of the residual edentulous ridge within the physiologic limits of border tissues permits optimal distribution of functional forces to the denture foundation; and the retromolar pad represents the area of the denture foundation that is relatively resistant to the resorptive processes and thus capable of providing stable and predictable prosthesis support. In consideration of the first theory, Tauchi et al[180] conducted an in vivo investigation to quantify force distribution secondary to occlusal load application relative to denture base extension in mandibular Kennedy class 1 and 2 prostheses.

A convenience sample of 7 participants (mean 70 years of age; age range 62 to 80 years of age; 3 men, 4 women) with Kennedy class 1 and 2 partial edentulism were enrolled in the study. Each participant received an experimental mandibular RPD containing 3 calibrated load cells to measure occlusal force application, abutment loading, and residual ridge loading. Four denture base lengths were evaluated through sequential shortening of the original (control) denture base; full length covering the retromolar pad (control), and 3 mm shorter, 6 mm shorter, and 9 mm shorter than control. With the control RPDs in place, the participants were guided to closure 5 times, and forces were recorded. The denture bases were then shortened 3 mm, the prostheses replaced, and the participants again guided to closure for force measurements. This experimental sequence was repeated for the 6-mm and 9-mm base adjustments.

The results indicated that for all participants and all denture base lengths, the forces distributed to the edentulous ridge increased in proportion with the applied occlusal loads. However, 1-way analysis of variance (α=.05) revealed no significant difference among the 4 denture base lengths relative to force distribution.

Based on these findings, the authors suggested that severe under-extension of an RPD denture base does not appear to overload the associated denture supporting tissues. However, limitations imposed by the experimental protocol (small number of participants and short-term experimental function/wear of prostheses) prohibited more robust conclusions. Within these limitations, the authors concluded that denture base coverage of the retromolar pad has little influence on force distribution originating from occlusal loads.

Conventional fixed prosthodontics

Contemporary dental patients expect both esthetic and durable fixed prosthodontic restorations, particularly when the rehabilitation of anterior teeth is required. With near continuous modification of ceramic materials, boding agents, and luting technology being reported, the practitioners' ability to provide sound evidence-based fixed prosthodontic therapy on natural teeth is challenging to say the least. With this in mind, Sailer et al[181] presented a systematic review addressing the long-term survival of metal ceramic and ceramic tooth-supported single crowns and the incidence of biological, technical, and esthetic complications.

The professional literature was searched for clinical studies focusing on tooth-supported single crowns with a mean follow-up of at least 3 years. Hand searching and inclusion of data from a previous systematic review complimented data acquisition. Survival and complication rates were analyzed using the robust Poisson regression models to obtain summary estimates of 5-year proportions.

The initial literature search identified 580 titles. Application exclusion/inclusion criteria and the addition of articles from a previous systematic review published by

this group of authors yielded 67 studies (published 1990 to 2013) detailing 4663 metal ceramic (from 17 studies) and 9434 ceramic single crowns (from 54 studies). Meta-analysis indicated a 94.7% 5-year estimated survival rate for metal ceramic single crowns. This 5-year survival rate was found to be similar to that of leucite or lithium-disilicate reinforced glass ceramic single crowns (96.6%), glass-infiltrated alumina single crowns (94.6%), and densely sintered alumina (96%) and zirconia (92,1%) single crowns. In contrast, 5-year survival rates for feldspathic/silica-based ceramic crowns were lower ($P<.001$).

Comparing restoration locations, feldspathic/silica-based ceramic and zirconia exhibited significantly lower survival rates in posterior regions ($P<.001$), whereas the other crown types performed better and similarly. Densely sintered zirconia single crowns suffered veneer ceramic fractures and failed cement retention more than metal ceramic single crowns ($P<.001$). Substructure fracture rates affected ceramic more than metal ceramic restorations.

The authors concluded that survival rates for most ceramic SC systems were similar to those reported for metal ceramic single crowns in both the anterior and posterior regions. Weaker feldspathic/silica-based ceramics should be limited to anterior applications. Veneered zirconia single crowns should not be considered as a primary option because of a high incidence of technical problems.

An ongoing evolution in materials science has resulted in new high-strength ceramics suitable for the fabrication of fixed partial dentures (FPDs). These new materials appear to satisfy esthetic demands for anterior applications. Long-term data for the performance of these new ceramic materials are now available in the professional literature. As a continuation of the previously discussed article by the same authors, Pjetursson et al[182] presented a second systematic review addressing the long-term survival of metal ceramic and ceramic tooth-supported FPDs and the incidence of biological, technical, and esthetic complications.

The professional literature was searched for clinical studies focusing on tooth-supported FPDs with a mean follow-up of at least 3 years. Hand searching and the inclusion of 10 studies from a previous systematic review supplemented conventional data acquisition. Survival and complication rates were analyzed using the robust Poisson regression models to obtain summary estimates of 5-year proportions.

The initial literature search identified 580 titles. Application exclusion/inclusion criteria and the addition of articles from a previous systematic review published by this group of authors yielded 40 studies detailing 1796 metal ceramic (from 15 studies) and 1110 ceramic FPDs (from 28 studies). Meta-analysis indicated a 5-year estimated survival rate of 94.4% for metal ceramic FPDs. This 5-year survival rate was found statistically similar ($P>.05$) to that of reinforced glass ceramic FDPs (89.1%) and densely sintered zirconia FDPs (90.4%) but significantly greater ($P<.05$) than that for glass-infiltrated alumina FDPs (86.2%).

Compared with metal ceramic FPDs, densely sintered zirconia FPDs experienced a higher incidence of caries. Compared with metal ceramic (0.6%) and densely sintered zirconia (1.9%) FPDs, reinforced glass ceramic (8.0%), and glass-infiltrated alumina (12.9%) FPDs experience more framework fractures at 5 years in function. Importantly, the incidence of veneer ceramic fractures ($P=.018$) and loss of retention ($P=.028$) were significantly greater for densely sintered zirconia FDPs than for all other FPD types.

The authors caution that when interpreting results, one should consider that the mean observation period was on average 7.0 years for metal ceramic FDPs and only 4.7 years for ceramic FDPs. If annual failure rates were greater in later years of restoration performance, then restoration types with longer follow-up periods would reflect greater average annual failure rates. To reduce the impact of such a bias, the results of the present analysis were restricted to 5-year survival estimates.

The authors concluded that metal ceramic FDPs had lower failure rates then ceramic FDPs after a mean observation period of at least 3 years. Framework fractures were frequently reported for reinforced glass ceramic and glass-infiltrated alumina FDPs. Densely sintered zirconia was significantly more stable as framework material compared with other ceramic alternatives, but suffered from secondary caries, loss of retention, and fracture/chipping of veneering ceramic. Continued improvement of available ceramic systems is necessary.

Management of a coronal tooth damaged using endodontic therapy, cast post and core, and complete-coverage coronal restoration is generally considered sound treatment. However, other treatment options are often available. Data are lacking on the survival of teeth treated with cast post and core restorations observed for more than 10 years. While crown survival rates for this treatment approach have been reported, tooth survival rates as scarce. Raedel et al[183] sought to remedy this shortfall by reporting tooth-level survival rates for cast post and core therapy with follow-up observation of more than 10 years, highlighting associated clinical parameters and potential influences on survival.

A retrospective evaluation was conducted on all cast post and cores inserted by predoctoral students or licensed dentists in a single university clinic between 1992 and 2011. A Kaplan-Meier survival analysis was carried out using tooth extraction as the target event. If the tooth in question was not extracted, the end of the observation period was set to the patient's last recorded

dental examination. The survival curves for different tooth types, the presence or absence of adjacent teeth, and the prosthetic restoration of the respective jaws were compared (log-rank test, α=.05). A multivariate stepwise Cox regression model was calculated to estimate the influence of the independent variable.

The data extracted for clinical records included a total of 717 cast post and cores in 343 patients (mean 57 years of age; age range 19 to 91). Tooth distribution was 33% premolars, 25% canines, 22% incisors, and 20% molars. Mean survival time was 13.5 years (range 12.8 to 14.2 years). Estimated 5-year survival rate was 86.9%, and estimated 10-year survival was 75.7%.

The results indicated that significantly reduced survival times were found for canines (11.9 years) and premolars (13.4 years) compared with molars (14.1 years); no adjacent teeth (10.6 years) compared with at least 1 adjacent tooth (13.8 years); and presence of conventional removable partial dentures (12.5 years) compared with crowns/fixed partial dentures (13.9 years). The poorest survival time was found for abutments of double crown-retained removable partial dentures (9.8 years). The existence of at least 1 adjacent tooth positively influences survival, whereas the tooth types, incisor, canine, and premolar, negatively influenced survival.

The authors concluded that cast post and cores have acceptable long-term survival. When considering the use of a cast post and core, it is prudent to investigate the many factors that may influence the survival of the proposed restoration. Considering these factors during treatment planning may increase the long-term success of restorations. More recently, conventional cast post and cores have been replaced by fiber-reinforced composite posts or adhesively-retained prefabricated metal posts. Whether these materials can achieve similar long-term survival rates has yet to be demonstrated.

Bacterial biofilms that form on dental hard tissues, oral soft tissues, dental restorative materials, and prosthetic devices contribute to the formation and progression of dental caries. During clinical restorative therapy, cariogenic exposure of prepared tooth structure to the oral environment may range from a few minutes to a few hours (direct restorative procedures) or longer (indirect restorative procedures). Further cariogenic exposures may relate to bacterial contamination beneath leaking restorations, long-term deteriorating provisional restorations, and biofilm-induced cementation failure.

In an effort to identify mechanisms for biofilm disruption/elimination prior to definitive coronal restoration placement, Torresyap et al[184] provided a single-patient clinical report documenting characteristics of the biofilms formed under a cemented restoration. A 62-year-old man presented requiring fixed prosthodontic restorations. Despite its poor prognosis (due to severe AL), the patient consented to have a mandibular second molar prepared and restored with a complete-coverage gold crown that was extracted following 6 months of oral function, and evaluated for biofilm contaminations.

This mandibular second molar was subjected to the following therapy: preparation, interim restoration, fine pumice cleaning/polishing of prepared tooth structure, assessment of definitive crown fit and occlusion, airborne-particle abrasion and steam cleaning of the gold crown, zinc phosphate cementation, and removal of excess cement. Upon extraction, the restored tooth was prepared/sectioned for confocal laser scanning microscopy evaluation facilitated by fluorescence in situ hybridization. The resultant tooth fragments were observed using SEM.

The findings indicated the presence of biofilms close to external restoration margins and within the cement layer between the gold crown and prepared tooth. The identified biofilm consisted of 2 distinct strata: an inner calcified layer and an outer developing layer. The existence of established biofilms in different areas within the restored complex may have detrimental consequences, including recurrent decay-associated restoration failure and cement failure secondary to bacterial/biofilm contaminates introduced during restoration placement. Based on findings, the authors suggested the need to develop new cementation protocols targeting the disruption of biofilms prior to definitive restoration placement.

General implant prosthodontic considerations

The ability to anticipate biological and biomechanical outcomes of dental interventions is essential for predictable and successful patient management. Recognizing and mitigating high-risk therapeutic conditions permits informed decision making and optimal treatment planning. As philosophies of treatment change over time, a periodic review of concepts is necessary to refine techniques and eliminate unnecessary procedures, forming a basis for improved care. With this in mind, Chrcanovic et al[185] conducted a systematic review and meta-analysis of prospective and retrospective studies to compare platform-switched and platform-matched dental implants with respect to survival rates, postoperative infection, and marginal bone loss was assessed relative to treatment follow-up periods.

An initial electronic search of major databases supplemented by manual searching of 22 relevant professional journals yielded 2907 articles. Application of inclusion/exclusion criteria reduced the list to 28 publications (18 randomized controlled trials, 6 controlled clinical trials, and 4 retrospective analyses), 18 of which were included in the meta-analysis. Accumulated data comprised a total of 1216 platform-switched implant-abutment interfaces (16 failures [1.32%]) and 1157 platform-matched implant-abutment interfaces

(13 failures [1.12%]). No implant failures were reported in 20 of the studies reviewed. Less marginal bone loss loss was reported at platform-switched implants (mean difference of −0.29 mm; $P<.001$). This difference between platform-switched and platform-matched increased with follow-up ($P=.001$) and with increasing platform mismatch ($P=.001$). Too few studies provided information on implant failure and postoperative infections, therefore prohibiting meta-analyses for these outcomes.

The authors suggested that, based on the studies reviewed, there was significantly less marginal bone loss at platform-switched implants than at platform-matched implants. However, the results of the present review should be interpreted with caution because of the presence of uncontrolled confounding factors, experimental/treatment heterogeneity (delayed versus immediate implant placement, grafting versus nongrafting, different healing periods, different prosthetic configurations, different opposing dentitions, splinted versus unsplinted), and short follow-up periods in the studies reviewed.

Dental implant treatment failure may be caused by failure of retentive screw joints. Excessive functional and parafunctional loads encountered in the stomatognathic system, or inappropriate/unstable retentive screw preloads, may lead to abutment screw loosening or fracture, ultimately contributing to catastrophic biomechanical failure of the implant restoration. To investigate implant screw joint stability, Lepesqueur et al[186] studied torque maintenance during in vitro mechanical cycling of dry lubricated abutment screws coated with either diamond-like carbon (DLC) or diamond-like carbon doped (CD) with diamond nanoparticles (CD-DLC) in external hexagon and internal hexagon implant-abutment joints.

Sixty screw-fastened implant-abutment pairs were randomly distributed to 6 experimental groups according to 2 variables: connection interface (external hexagon versus internal hexagon) and titanium alloy abutment screw coating (uncoated versus DLC versus CD-DLC). DLC and CD-DLC screw coating was accomplished by plasma-enhanced chemical vapor deposition. A calibrated digital torque wrench was used to achieve manufacturer recommended abutment screw torque specifications (20 Ncm for internal hexagon implants and 30 Ncm for external hexagon implants). All screws were retightened to specifications 10 minutes after initial tightening. In standardized fashion, all implant-abutment complexes were mounted into polyurethane resin blocks. Base metal alloy crowns with screw access holes (to facilitate screw torque/detorque testing) were cemented to abutments using an interim cement.

Mechanical fatigue loading was applied to specimens in a test frame using an average force of 133 N at an eccentric contact distance of 3 mm from the implant center and a frequency of 4 Hz, resulting in 1×10^6 cycles (representing approximately 12 months of function) at a temperature of 37°C. After loading, abutment screws were subjected to reverse torque measurements, and torque maintenance was calculated. Representative screws from each experimental group were evaluated for structural alterations using scanning electron microscopy. Statistical analysis was performed using 1-way ANOVA and the Tukey test ($\alpha=.05$).

The results demonstrated that the highest torque value was maintained in external hexagon joints fastened with uncoated screws ($P<.001$), an intriguing observation given the reported superiority of internal connection geometries on screw joint stability. No differences were observed between groups with and without screw coatings relative to torque maintenance in internal hexagon connections ($P=.548$).

The authors concluded that, compared with standard titanium alloy screws, the use of abutment screws dry lubricated with DLC and CD-DLC demonstrated no improvement in torque maintenance in external hexagon and internal hexagon implant connections. However, in future investigations, the surface protective effect of these coatings, as seen microscopically, may prove valuable under different loading circumstances.

Accurate prosthesis fit, for both implant and conventionally supported restorations, is considered a desirable goal in prosthodontics. The degree to which this goal is achieved is believed to determine, in part, the durable success of involved prostheses. An early step in the fabrication of accurately fitting indirect dental restorations is generation of an accurate digital dental cast using intraoral scanning technology, or an accurate hard dental cast using conventional impression procedures. Lin et al[187] sought to compare the accuracy of these 2 cast- generating processes using a partially edentulous mandibular model incorporating 2 implants placed at either parallel or divergent relative axial trajectories.

Four customized, partially edentulous (Kennedy class 2), epoxy resin master models were fabricated. Two implant analogs positioned in the posterior edentulous space of each model varied only in their relative axial trajectories (parallel or 0 degrees, and 15, 30, and 45 degrees divergent). For the conventional (control) group, 10 conventional impressions were made on each experimental model (custom trays, open-tray impression copings, and polyvinyl siloxane material), and Type IV dental stone casts were fabricated. For the digital (test) group, 10 digital impressions were made on each experimental model (2-piece scannable impression copings and an intraoral digital scanner), and milled polyurethane casts were fabricated. All 4 experimental models, 40 conventional control casts, and 40 digital test casts were scanned and digitized so that resulting data sets could be electronically compared. Three-dimensional

deviations in distance and angulation between implant analog positions in experimental models and corresponding casts were identified and analyzed.

Generally, the results indicated that implant divergence did not affect the accuracy of the stone casts created from conventional impressions. However, implant divergence significantly affected the accuracy of the milled test casts created from digital impressions. A decreasing linear trend in deviations for both distance and angulation measurements suggested that the digital impression technique improved as implant divergence increased. At 0 and 15 degrees of divergence, the milled test casts were significantly less accurate. At 30 and 45 degrees of divergence, the milled test casts were either statistically similar or only marginally less accurate than the conventional control casts.

The authors concluded that, in the in vitro investigation, digital impressions produced less accurate casts than conventional impressions using a 2-implant, partially edentulous, variable implant trajectory, test scenario. Because accurate prosthesis fit is an important objective in prosthodontics, verification and cast accuracy appears essential when using digital impression technology.

Periimplantitis has been described as infection with suppuration associated with clinically significant progressive periimplant crestal bone loss occurring after initial remodeling. The cause of this condition is considered multifactorial and includes implant factors (material, surface properties, design), clinician factors (surgical and prosthodontic experience, skill), and patient factors (systemic disease, medication, oral disease, oral hygiene, smoking, bone quality). Recently, the absence of prosthetic factors from the multifactorial list of etiologies has been questioned. To investigate potential prosthetic factors, Pesce et al[188] systematically reviewed the available literature to elucidate the role of cement excess and ill-fitting prosthetic components in the development of periimplantitis.

An electronic search of major professional literature databases was accomplished. Article selection was limited to cohort and case-control studies with at least 10 participants per experimental group and at least 6 months of follow-up. Human randomized controlled clinical trials are not available as they would be unethical in this area of inquiry. Periimplantitis and implant failure were considered primary and secondary outcome variables.

An initial literature search produced 275 titles. Application of inclusion/exclusion criteria eliminated 252 articles. An additional 23 articles were eliminated after full text review. Thus only 2 articles were determined eligible for the present systematic review. These reports indicated a correlation between cement excess and the presence of periimplant disease, particularly in patients with a history of periodontal disease. After the removal of excess cement, disease symptoms resolved around most implants.

Experimental heterogeneity prohibited meta-analysis on the issue of excess cement as an etiologic factor in periimplantitis. No articles of adequate quality were identified addressing implant component misfit as an etiologic factor in periimplantitis.

The authors concluded that scientific articles on prosthetic risk factors for periimplantitis are scarce. Although the 2 reports identified on residual excess cement have a high risk for bias, cement excess seems associated with mucositis, and possibly with periimplantitis, especially in patients with a history of periodontal disease. Well-designed human clinical trials on periimplantitis are difficult to conduct because of ethical limitations. However, the authors indicated the need for a more rigorous approach in future studies.

Implant removable prosthodontics

Conventional complete dentures and implant-retained overdentures likely transfer dynamic functional loads to the residual edentulous ridges differently. Over time, this difference in load transfer may influence residual ridge resorption. Ahmad et al[189] studied and compared mandibular residual ridge resorption associated with complete dentures and implant-retained overdentures over 1 year of function. Hydrostatic stress, contact surface deformation, and strain energy absorption of the mandibular denture foundation were assessed as biomechanical factors in residual ridge resorption.

Twenty-nine patients with edentulism participated in this study (mean 67 years of age; age range 52 to 79 years of age; 14 men, 15 women). Based on clinical needs, 20 participants were assigned to the implant-retained overdenture group and 9 to the complete denture group. All participants received pretreatment cone beam computed tomography (CBCT) scans to register baseline mandibular residual ridge resorption and mucosa thickness. Participants in the implant-retained overdenture group were provided 2 dental implants (mandibular canine regions), mandibular implant-retained overdentures (telescopic attachments), and maxillary complete dentures. Participants in the complete denture group were provided conventional complete dentures. Unilateral maximum occlusal forces were recorded.

Pretreatment and 1-year post-treatment CBCT scans from a representative participant in each experimental group were converted to 3D finite element analysis (FEA) models. Comparison of pretreatment and post-treatment CBCTs yielded qualitative and quantitative information on residual ridge resorption. Hydrostatic stresses distribution, contact surface deformation, and strain energy absorption in the soft tissues of the denture foundation were correlated with changes in residual ridge resorption for participants with and without implants.

The results indicated that mean occlusal force for implant-retained overdenture participants (N=110) was nearly twice that recorded for complete denture participants (N=63). Similarly, the contact surface deformation of ridge mucosa was 2 times greater for implant-retained overdentures (0.32 mm) than for complete dentures (0.16 mm). Again in like fashion, the amount of residual ridge resorption was also 2 times greater for implant-retained overdentures (–3.8%) than the complete denture (–1.9%). residual ridge resorption identified in impant-retained overdenture participants was predominantly seen in molar regions (ridge crest) and premolar regions (lingual). This is consistent with theoretical rotation of the prosthesis around an interimplant axis. Considering the differences in the occlusal force recorded for impant-retained overdenture and complete denture participants, hydrostatic stress within the denture foundation mucosa correlated well with residual ridge resorption mapping over the 1-year interval of treatment.

Based on research methods applied, the authors concluded that implant-retained overdentures resulted in at least twice the residual ridge resorption as compared with complete dentures. This may result from higher hydrostatic stress and less effective energy absorption capabilities of the denture foundation mucosa associated with implant-retained overdenture. Additionally, implant-retained overdenture participants were capable of greater occlusal force, which could potentially concentrate hydrostatic stress and cause greater residual ridge resorption than a conventional complete denture. It appears that mucosal hydrostatic stress plays a significant role in residual ridge resorption and that the magnitude of residual ridge resorption is influenced by the occlusal force exerted on the denture, the resultant contact surface deformation in the mucosa, and the strain energy absorption capabilities of the mucosa underneath prostheses.

Patients with edentulism provided with new complete dentures have reported improved overall satisfaction, esthetics, and speech. However, functional outcomes are often unsatisfactory. The addition of dental implants to facilitate prosthesis support, retention, and stability is generally believed to impact oral function as well. A variety of methods have been used to assess oral function as a parameter of edentulous patient satisfaction. To date, these methods have not been systematically reviewed. Boven et al[190] presented a systematic review addressing edentulous patient satisfaction with implant overdentures before treatment and after a minimum 1-year observational period. Patient satisfaction relative to masticatory performance, occlusal force, and nutritional status were of interest.

A thorough search of professional literature using major databases was accomplished to identify prospective publications describing at least 10 edentulous patient therapies with at least 1 year of follow-up assessment in the area of interest. The initial search identified 920 titles. Application of inclusion/exclusion criteria and full-text analysis narrowed usable articles to 53, most of which reported on mandibular implant overdentures.

The results demonstrated that patients wearing implant overdentures were highly satisfied with prosthesis comfort. However, satisfaction with comfort was not always accompanied by improvement in general QoL or health-related QoL. With respect to oral function, results indicated that occlusal force improved, masseter thickness increased, and muscle activity at rest decreased. The patients believed that their mastication function improved and that they could eat foods of tougher consistency. However, no changes were noted in dietary intake, BMI, or blood markers for nutritional intake. In reports detailing trials with longer-term follow-up, improvements recorded after 1 year decreased slightly with time.

The authors concluded that converting edentulous complete denture wearers to IOD wearers improves masticatory performance, increases maximum occlusal force, and improves patient satisfaction. The effect on QoL is uncertain, and there appears to be no beneficial impact on nutritional status. Unfortunately, since most existing reports detail outcomes with mandibular implant overdentures, information on maxillary implant overdentures is limited. Because the majority of currently published research addresses mandibular implant overdentures followed for 1 year, the authors recommend that future research focus on longer-term results and maxillary implant overdentures.

Excessive functional movements of extension base RPDs has been associated with edentulous ridge resorption, damage to abutments, reduced masticatory efficiency, decreased patient comfort, and occlusal instability. Placement of a single posterior dental implant to support and stabilize the RPD extension base during functional loading has been recommended. Zancope et al[191] endeavored to systematically evaluate current evidence detailing placement of a dental implant to provide support for extension base RPDs in order to improve patient satisfaction and clinical prosthesis performance.

The professional literature was thoroughly searched for prospective controlled clinical trials and clinical studies reporting patient satisfaction and prosthesis performance. A randomized controlled trial filter was not applied since no such trials currently exist. No restriction of follow-up length was imposed. Initial electronic and hand searches identified 246 reports. Application of inclusion/exclusion criteria and full-text analysis narrowed usable material to 15 studies for data extraction. Seven were retrospective studies, 1 a crossover pilot study, 2 case series, 2 paired clinical studies, and 3 case reports, yielding low scientific methodological quality on which to base conclusions.

Results were drawn from a total of 163 patients wearing mandibular Kennedy class 1 or 2 RPDs supported by a single implant per edentulous space. Implant survival rate was 99.13%, follow-up periods ranged from 0.5 to 120 months, and marginal periimplant bone loss ranged from 0 to 1.4 mm. Periodontal status and survival of natural tooth abutments were inadequately described. The implants were fitted with healing abutments (for prosthesis support) or resilient attachments (for support and retention). Visual analog scales, patient narrative reports, and masticatory performance were used to record patient satisfaction.

The authors concluded that the use of a dental implant to support and stabilize extension bases of Kennedy class 1 and 2 RPDs appears to yield favorable results. Patient satisfaction, comfort, and masticatory performance increase, while implant survival rate is not impaired. The use of only 2 implants (Kennedy class 1) and associated lower cost may make this treatment more accessible for patients. The incorporation of an additional means for extension base retention may further improve patient satisfaction. The authors were careful to mention that long-term, prospective, controlled, clinical studies with homogeneous methodology are lacking and optimal clinical protocols remain ill defined. Despite favorable existing reports, critical evaluation of natural tooth abutments subjected to this form of prosthodontic therapy must be accomplished.

Despite consensus statements that a 2-implant mandibular overdenture is the current standard of care for mandibular edentulism, no definitive evidence exists supporting a universally accepted standard, with or without dental implants. To investigate optimal care, Bryant et al[192] carried out a randomized clinical trial comparing outcomes for edentulous patients treated with 1 or 2 implants placed symmetrically in the anterior mandible to retain a complete mandibular overdenture.

Eighty-six healthy edentulous participants (mean: 67 years of age) stratified by age, sex, and edentulous ridge dimensions were randomly allocated to 2 treatment groups. Group 1 received 1 dental implant placed in the mandibular midline. Group 2 received 2 dental implants placed in the mandibular canine areas. Prosthodontic restoration involved maxillary conventional complete dentures and mandibular complete overdentures with ball attachments. Satisfaction was self-assessed by participants on a visual analog scale at baseline prior to implant placement, at 2 months, and at 1, 3, and 5 years after prosthesis placement. Implant survival and prosthodontic maintenance were assessed clinically. Twenty-nine participants from group 1 and 33 participants from group 2 were available for 5-year follow-up examination.

At 2 months, satisfaction with implant overdentures was significantly greater than baseline in both groups ($P<.001$) and remained significantly greater through the 5-year follow-up point ($P=.001$), demonstrating no difference between groups ($P=.32$). During the follow-up course, group 1 experienced no implant failures, but group 2 experienced 5 implant failures before loading. Most prostheses required maintenance. Significant associations between the number of maintenance events and treatment groups could not be identified, although group 1 tended to have proportionately more replacement dentures, relines, and denture fractured (typically adjacent to the attachment).

The authors concluded that no significant differences existed after 5 years between edentulous mandibles rehabilitated with 1- or 2-implant overdentures. However, an insignificant trend in greater maintenance needs was associated with 1-implant overdentures. An acceptable standard of care should take into account the affordability of therapy, and clinicians should explore the costs associated with implant dentures and the possibility that a 1-implant overdenture may offer a more universally accessible alternative for managing mandibular edentulism.

Implant fixed prosthodontics

Cement-induced periimplant inflammation is a common clinical concern with significant clinical impact. The potential of different cements commonly used in implant dentistry to efficiently and effectively accumulate bacterial biofilms has not yet been reported. Papavasileiou et al[193] examined subgingival periimplant biofilm formation on various luting agents under clinically simulated in situ conditions.

A convenience sample of 17 participants possessing 2 or more dental implants with healing abutments were enrolled in the study. A round bur was used to prepare 2 cavities (2-mm diameter × 2-mm deep) on opposite sides of the healing abutment axial surfaces in subgingival locations. Cement specimens were loaded into each cavity according to the manufacturer's instructions. Cements investigated included TempBond, Harvard Cement, RelyX Unicem, and Panavia F 2.0. TempBond-Harvard specimens and RelyX-Panavia specimens were always applied in pairs at the opposite sides of the same healing abutments. These test healing abutments were placed at healed sites assuring subgingival location of cement specimens. Healing abutments were recovered after 10 days and evaluated by SEM.

The results identified large areas of biofilm colonization on all cement surfaces (84.0 to 91.6% coverage) and cement-titanium cavosurface margins (83.3% to 89.4% coverage). No statistically significant differences in biofilm coverage were observed. Conversely, significantly less biofilm colonization was found on the smooth subgingival titanium surfaces of healing abutments.

A proposed benefit of cemented implant restorations, compared with screw retention, is placement of

restorative margins safely distant from the alveolar crest by incorporating suitable abutment design. With the escape of excess cement from this alleged biologically safe margin location into the periimplant crevice and subsequent biofilm formation, the perceived benefit of cemented restorations is not realized. Additionally, the generalized total colonization of the cement-titanium margin test abutments suggests great challenge when attempting to minimize subgingival margin discrepancies in a clinical setting.

Generally, the retention of fixed dental implant restorations may be achieved using screws or cement. Clinical and laboratory factors such as bone volume and resorptive pattern, implant position/trajectory, prosthesis retrievability and maintenance, esthetics, phonetics, occlusion, ease of fabrication, cleansability, and cost (to name just a few) may influence the decision to fabricate restoration for screw or cement retention. Unfortunately only insufficient, unbiased evidence currently exists on which to base this decision. With the hope of bringing clarity to this challenging issue, Ma and Fenton[194] systematically reviewed the existing literature to identify prosthodontic outcomes for screw- and cement-retained implant prostheses with respect to maintenance and complications.

The professional literature electronically was thoroughly searched. Initial results yielded 1432 titles, of which 103 were eligible for full-text evaluation. Application of inclusion/exclusion criteria and full-text analysis narrowed the published material to 54 articles. Manual searching identified 8 additional studies. Only 6 randomized controlled trials were available.

Problems encountered included the lack of equivalent numbers of screw- and cement-retained single-implant crowns for comparison, use of different retention screw types, inadequate screw preloading information, use of a nonstandardized range of dental cements, general lack of rationale for cements used, general lack of rationale for the screw types used, and varying observational periods after placement. Some studies reported various prosthodontic maintenance/complication (screw loosening, porcelain fracture, loss of retention, and esthetic concerns), whereas others failed to report any prosthodontic maintenance issues during the observation periods. More recent studies did not report any incidence of screw loosening. Only 2 studies provided standardized criteria for reporting prosthodontic maintenance/complication issues.

The authors concluded that with inadequate available information and nonhomogeneous study designs and reporting, it was difficult, if not impossible, to compare prosthodontic outcomes between screw- and cement-retained fixed implant restorations. Both of the retention mechanisms appear to have prosthodontic maintenance/complication issues that must be considered when prescribing restoration design. Standardized criteria should be developed and used when reporting prosthodontic maintenance/complication issues to permit better data management and review in the future. Currently, the selection of screw- or cement-retention for fixed implant restorations is based on anecdotal information or personal preference rather than founded in credible scientific data.

Prosthodontic materials

Laboratory fabrication of indirect dental restorations typically necessitates intraoral adjustments before restoration placement. Routinely, diamond rotary instruments of varying grit are used to refine the intaglio surface, proximal surfaces, and occlusal surface to assure optimal restoration fit and function. In accomplishing these adjustments, the restorative material may be compromised. Coldea et al[195] analyzed the damage tolerance of popular indirect restorative materials by grinding on standardized specimens with diamond rotary instruments to simulate clinically relevant adjustments.

Seven commercially available restorative materials were analyzed, including 4 computer-aided design-computer-aided manufactured (CAD-CAM) ceramics (MarkII, IPS e.max CAD, In-Ceram YZ, and In-Ceram Alumina), 1 veneering ceramic (VM 9), and 2 interpenetrating phase composites (ENAMIC and PICN). In-Ceram Alumina was examined without a veneering layer. ENAMIC (75 vol.% ceramic, 25 vol.% polymer) and PICN (69 vol.% ceramic and 31 vol.% polymer) are interpenetrating phase composites with 2 continuous networks of ceramic and polymer.

Forty bend bars of each material were fabricated according to the manufacturer's instructions. Bar specimens were lapped and polished to 18×4×1.2 mm, and the edges were chamfered. Generation firing of the In-Ceram YZ specimens accomplished according to the manufacturer's instructions.

Initial flexural strength was determined in 3-point-bending on 10 specimens. Elastic modulus and Poisson ratio were calculated using the resonant frequency method. To simulate "adjustments," the remaining specimens were divided into 6 groups (n=5) and subjected to standardized grinding with 3 different diamond grit rotary instruments (coarse, medium, and extra fine) using 2 grinding directions (transverse and longitudinal). Adjusted specimens were loaded to fracture and analyzed by SEM.

The results indicated that, except for In-Ceram YZ, the initial flexural strength of all tested materials decreased significantly secondary to diamond rotary instrument grinding/adjustments (transverse and longitudinal directions). The order of damage tolerance (greatest to least) for tested materials is PICN > ENAMIC > Mark II > VM 9 > In-Ceram Alumina > IPS e.max CAD.

Transverse adjustment of In-Ceram YZ specimens with course grit instruments resulted in a strength value of 1196.9 MPa. Compared with its initial flexural strength of 1222.1 MPa, In-Ceram YZ exhibited no strength degradation upon adjustment (P=.76). Of the other materials, the least strength degradation was demonstrated by VM 9 (7.79%) and ENAMIC (9.18%) upon longitudinal grinding with extra fine and medium grit rotary instruments, respectively. The greatest strength degradation was demonstrated by emax CAD upon transverse adjustment with course and medium grit rotary instruments. Generally, the materials demonstrated greater flexural strength degradation upon transverse as compared with longitudinal adjustment.

The authors concluded that restorative material damage tolerance to adjustment depends on specific mechanical properties and the adjustment procedures used. For example, the novel interpenetrating phase composites ENAMIC and PICN exhibit a high damage tolerance to typical clinical adjustment procedure. Adjustment of the materials tested here with course diamond rotary instruments degrades material strength more than adjustment with extra fine instruments. The authors indicate that outcomes of these simulated adjustment protocols can be adopted clinically in terms of materials selection and corresponding instrument and adjustment parameters.

Given the fluid-rich (saliva) oral environment, an ideal dental impression material in the unset state would be hydrophilic. Of the most common modern elastomeric impression materials, polyether (PE) is qualified as relatively hydrophilic, while polyvinyl siloxane (PVS) is decidedly hydrophobic. Improved wettability can be achieved by adding nonionic surfactants to PVS materials to increase hydrophilicity. To investigate performance of contemporary impression materials, Menees et al[196] compared the hydrophilicity of 7 different unset elastomeric impression materials during polymerization by measuring contact angles at 5 time points from the start of mixing with 2 adherents (water and saliva).

The 7 impression materials investigated included 2 conventional brands of PVS (Aquasil and Take 1), 2 PVSs modified with novel surfactants (Imprint 4 and Panasil), a PE (Impregum), and 2 hybrids (Identium and EXA'lence). A specimen former was used to produce 24-mm-diameter wafers of each impression material 2-mm thick. A 5 μL droplet of distilled water or saliva was dispensed onto the specimens' surface 25 seconds (t_0) after the start of mix. Using a digital microscope, contact angle measurements were made at t_0, t_1 (27 seconds), t_2 (32 seconds), t_3 (50% working time), and t_4 (95% working time). The data were analyzed with a generalized linear mixed model analysis, individual 1-way ANOVA, and Tukey honest significant difference (HSD) post hoc tests (α=.05).

With water as the adherent, the results indicated that impression materials grouped into 3 general categories at all time-points: modified PVS (Imprint 4 and Panasil) and a hybrid (Identium), produced the lowest contact angles, PE (Impregum) was intermediate, and conventional PVS (Aquasil and Take 1) and the other hybrid (EXA'lence) produced the highest contact angles. When saliva served as the adherent, a hybrid (Identium), the PE (Impregum), and a modified PVS (Imprint 4) yielded the lowest contact angles at most time points.

The authors concluded that surfactant-modified PVS and a hybrid impression material were most hydrophilic with a water adherent. However, for saliva, the hybrid and PE materials appeared most hydrophilic. Saliva, unlike water, contains mucins and dissolved proteins and salts. The more saturated saliva solution may have interacted with surfactants in the modified PVS materials differently than did water, yielding less favorable wetting. PE materials, however, achieve hydrophilicity through their chemical structure, thus performing well with a saliva adherent. These finding indicate that saliva behaves differently than water in laboratory studies measurement wettability of contemporary unset elastomeric impression materials. The authors suggest that a potential continuation of this investigation might be to measure and compare levels of surfactant in salivary and aqueous adherents.

The use of interim polymeric fixed prosthodontic restorations is generally intended for short duration, transitional therapy. However, in more complicated treatments, a longer-term interim restoration phase is frequently indicated. In such situations, the structural durability, integrity, and 3D stability of interim restorations are important to clinical success, particularly in patients with the capacity for high occlusal load generation. Vaidyanathan et al[197] evaluated the short- to medium-term stability of representative interim resin materials using an in vitro protocol under controlled loading conditions in order to assess their stress relaxation behavior.

Five polymeric interim materials were examined: 2 acrylic resins (TRIM II and Alike) and 3 bis-acryl composite resins (Luxatemp, VersaTemp, and Temphase). Rectangular bar specimens (45×20×10 mm) were prepared (6 specimens per group). Stress relaxation tests were performed isothermally at 32°C, 37°C, and 42°C by programmed scanning under an applied constant strain (0.2%) using a dual cantilever clamp over a preoptimized time span (to a steady- state level) in a dynamic mechanical analyzer. Stress decay data with time, under constant applied strain, due to internal strain caused by molecular relaxation was systematically analyzed using important parameters derived from stress changes with time. The glass transition temperature of each material was also determined.

The results indicated significant differences in the stress relaxation for the materials studied, which may have significant bearing on material durability in medium- to longer-term clinical applications. Limited capacity for stress relaxation promotes molecular relaxation focused at defect sites, helping to prolong/prevent fracture propagation. Excessive stress relaxation may result in unacceptable dimensional change within the bulk material, material weakening, and loss of continued stress tolerance necessary for durable function. Relative to poly(methyl methacrylate) (PMMA; Alike) and the bisacryl composites studied here, poly(ethyl methacrylate) (PEMA; TRIM II) subjected to constant strain over a period of time showed high internal molecular (stress) relaxation effects. Thus PMMA and composite resins tolerate constant strain without excessive dissipation of applied stress.

The authors concluded that, compared with other resins tested, PEMA appeared to have inadequate functional durability for medium- to longer-term applications as a fixed prosthodontics interim restoration material. PEMA demonstrated internal strain caused by stress relaxation events that may lead to excessive dimensional instability.

In order to perform satisfactorily in the oral environment, fixed prosthodontics restorations must be fabricated using materials that demonstrate sufficient stability, durability, strength, and esthetic potential. Additionally, these materials must be biologically and biomechanically compatible within the oral cavity under expected function demands. With respect to occlusal function, fixed prosthodontics materials should induce limited wear of opposing natural tooth tissues. In an in vivo protocol, Mundhe et al[198] evaluated the wear of natural enamel against natural enamel, polished zirconia, and metal ceramic occlusal surfaces over a 1-year time period.

Ten patients (18 to 35 years of age) requiring 2 complete coronal coverage molar crowns, one on either side of the mandibular arch, and healthy teeth opposing planned restorations, were identified and enrolled in the study. Each participant received a single monolithic polished zirconia crown (LAVA, yttrium-stabilized zirconium oxide) and a single glazed metal ceramic crown (Ceramco 3, feldspathic porcelain). The teeth were prepared and crowns cemented (left side versus right side) according to a randomization list. The teeth were divided into 3 groups: enamel-enamel (control), zirconia-enamel, and porcelain-enamel.

To evaluate occlusal surface wear, PVS impressions were made of antagonist arches immediately after crown cementation (baseline) and 1-year thereafter. The resulting casts were scanned with a 3D white light scanner. Baseline scanned images were superimposed on corresponding 1-year images using 3D software. Linear and depth assessments of wear occurring on antagonist teeth were calculated. One-way repeated measures ANOVA was used to determine the overall significance of means among the 3 groups. Bonferroni correction was applied for pair-wise comparison.

The results indicated that occlusal wear of antagonist enamel 1 year after cementation of metal-ceramic crowns was 69.2 μm for premolars and 179.7 μm for molars, whereas against zirconia crowns, occlusal wear was 42.1 μm for premolars and 127.0 μm for molars. Occlusal wear of antagonist enamel opposing natural enamel was 17.3 μm for premolars and 35.1 μm for molars. Statistical evaluation ($P<.001$) of these findings indicated that (1) enamel wear opposing all 3 test surfaces was significant; (2) enamel wear opposing metal ceramics and zirconia was greater than enamel wear opposing enamel; (3) enamel wear opposing zirconia was less than enamel wear opposing metal ceramics; and (4) enamel wear opposing all 3 test surfaces was less on premolars than on molars.

The authors' main conclusion was that zirconia crowns were associated with less wear of antagonist enamel than metal ceramic crowns but more than natural enamel. The more favorable wear performance of zirconia may be related to superior physical properties and surface features (hardness, bend strength, fracture toughness, and density) compared with feldspathic porcelain, enabling zirconia to maintain a smooth surface with less potential for causing opposing wear. They also noted that zirconia used here was polished not glazed. Previous research indicated more favorable wear characteristics for polished zirconia.

The authors indicated that the small sample size and short observation period were limitations of this study. Additionally, the wear of the crown materials should be assessed in future studies.

OCCLUSION AND TEMPOROMANDIBULAR DISORDERS

Many interesting articles related to the field of occlusion and temporomandibular joint (TMJ) dysfunction were produced in 2015. Given that 3D imaging has become commonplace in the diagnosis and treatment of temporomandibular disorders, there were some significant articles related to both magnetic resonance imaging (MRI) and CBCT imaging. Morales and Cornelius[199] organized a comprehensive review article discussing an imaging approach to TMJ joint disorders. The following is a summary of that review article.

As an introduction, they state that temporomandibular disorders (TMDs) are a heterogeneous group of conditions involving the temporomandibular joint complex that might also involve the surrounding musculature and osseous components. TMD is the second most common musculoskeletal and neuromuscular condition

(after chronic low back pain) resulting in pain and disability with an annual cost estimated at $4 billion. Common symptoms include jaw pain or dysfunction, earache, headache, and facial pain. Multiple risk factors include trauma, anatomic factors (such as skeletal and occlusal relationship), pathophysiological factors (such as bone and connective tissue disorders, hormonal differences), and psychosocial factors (such as depression and anxiety). Controversy still exists for most of these factors, and the only consistent correlation is with sex and age. A known higher prevalence of TMD is found in women than in men, with ratios ranging from 2:1 to 8:1 in different studies. As it may relate to estrogen and is more common in premenopausal women, the incidence peaks in the second to fourth decade of life.

Internal derangement of the disk is the most common TMD and the most common finding on MRI of the TMJ. Internal derangement of the TMJ refers to an abnormal positional and functional relationship between the disk and mandibular condyle, articular eminence, and glenoid fossa. Common clinical findings include joint noise/clicking, crepitus, and joint locking. Degenerative osteoarthritis, or degenerative joint disease, is the second most common pathology, with higher prevalence in older age groups. Trauma is a frequent cause of TMJ morbidity. Less common pathology includes inflammatory arthritis (rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis), synovial chondromatosis, calcium pyrophosphate dehydrate deposition disease (CPPD), pigmented villonodular synovitis (PVNS), tumors, infection, and osteonecrosis.

In this context, an understanding of the relatively complex TMJ anatomy and dynamics and an awareness of less common but important pathology affecting the joint are paramount for radiologists interpreting head and neck imaging. Anatomically, TMJ disorder is separated into a superior and inferior compartment by the disk and its attachments. The disk has an anterior and posterior band with a thinner intermediate zone present at its center, giving the disk a biconcave appearance on sagittal views. The posterior band is thicker than the anterior band. The anterior and posterior bands are longer in the mediolateral than anteroposterior dimension. The posterior margin of the posterior band is called the "bilaminar zone," a rich neurovascular tissue, which is composed of superior and inferior layers. These retrodiscal layers serve as posterior attachments, blending with the joint capsule and temporal bone. Lateral attachments of the disk are also present, and they blend with the capsule and insert into the condylar neck. The components of the anterior attachment of the disk are variable. It is called "disk-capsular complex." There may or may not be fibers of the lateral pterygoid muscle (LPM) and tendon attachment to the anterior band of the disk and this complex.

The normal position of the disk can be evaluated by the location of the posterior band, which superiorly covers the condyle in the closed mouth position near the 12-o'clock position on the sagittal projection. The medial and lateral corners of the disk align with the condylar borders and do not bulge medially or laterally. The basic motion of the mandibular condyle has 2 components. The condyle first rotates and then translates anteriorly with respect to the temporal bone as the mouth is opened. The LPM contributes to jaw opening along with the medial pterygoid and masseter muscles while temporalis muscles facilitate jaw closure. The motion of the disk can be easily evaluated on MR imaging. As the condyle translates anteriorly, the disk should move into a position in between the condyle and the articular eminence with full contact of the intermediate zone. The disk does not move in the coronal plane when the joint is normal.

MRI is the best method for evaluating intra-articular processes; and given its high definition of the soft tissues, it is currently the gold standard for the diagnosis of disk disorders. Computed tomography is the best method of evaluating the osseous components. CBCT has shown comparable osseous detail to CT, with the advantage of a decreased radiation dose. The disadvantages are its increased noise and motion artifacts and the significant lack of definition of the soft tissues.

Imaging is usually indicated in patients in whom malocclusion or intra-articular abnormalities (joint noises or crepitus are noticed during examination or reported by the patient) are suspected. In addition, imaging is indicated in patients with trauma, swelling/infection, and failure of conservative treatment. In the setting of trauma, CT is the primary imaging modality, because it shows bone detail. CT is also particularly useful in the setting of surgical reconstruction, in the evaluation of calcified loose bodies and degenerative osteoarthritis, and in some patients with inflammatory-infectious entities and tumors. Generally, CT and MRI are complementary techniques. However, the importance of MRI and its correlation with clinical findings is becoming increasingly recognized, particularly in pathologies such as internal derangement or osteoarthritis.

A systematic approach to the interpretation of TMJ imaging is desirable. Even though disk abnormalities are the most common disorders in the evaluation of TMJ, other less common entities such as inflammatory arthritis, synovial osteochondromatosis, PVNS, tumors, infection, and osteonecrosis can affect the joint and should be recognized by the radiologist. Based on major anatomic structures, a systematic approach is offered beginning with disk attachments. When approaching the disk, it is necessary to describe its location, morphology, and function. As previously described, the normal location of the disk can be evaluated by the position of the

posterior band. The posterior band should lie immediately above the condylar head near the 12-o'clock position. Prior studies report an abnormal range of 10 degrees to 30 degrees (anterior or posterior) displacement from the 12-o'clock position on sagittal views. A definition of abnormal, at approximately 10 degrees from the 12-o'clock position, might result in the inclusion of a larger number of asymptomatic volunteers, while a definition of abnormal, beyond 30 degrees from the 12 o'clock position, would correlate better with the clinical symptoms of TMJ dysfunction. Others have pointed out the importance of the intermediate zone to evaluate disk displacement. The position of the disk is considered normal if the intermediate zone is located between the anterior-superior aspect of the condyle and the posterior-inferior aspect of the articular eminence; thus, disks located anterior to this position are considered abnormal. In fact, there appears to be an improved clinical correlation with the intermediate zone criterion as compared with criteria based in the posterior band location. Unfortunately, there is no overall consensus in the literature as to how much displacement is considered abnormal or when might become symptomatic.

Anterior disk displacement can be partial or complete. The term partial anterior displacement is used when the posterior band falls in the normal superior position covering the condyle in at least 1 section of the disk on sagittal images. Partial anterior displacement has been found in similar frequency in both symptomatic and normal volunteers. Therefore, its clinical significance is uncertain. However, complete anterior displacement is almost exclusive to symptomatic patients. A superimposed component of lateral or medial displacement may also be present when the disk is completely dislocated anteriorly. Rarely, can the disk demonstrate pure sideways displacement, that is, pure lateral or medial displacement. Posterior displacement is the rarest form of disk derangement and is usually associated with a locked joint.

In the setting of chronic internal derangement, the form of the disk is progressively altered. Early, slight thickening of the posterior edge of the disk can be depicted. Loss of the normal biconcave shape with a globular or biconvex appearance has also been described as an early degenerative change. Later, disk desiccation with a thin appearance is seen. Perforation of the disk or attachment is a sign of late stage internal derangement. In all patients with perforation, the disk demonstrates no recapture on open mouth views.

Evaluation of the function of the disk is the next step. When the disk is displaced on a closed mouth view, the open mouth views can demonstrate recapture of the disk to a normal position in between the condyle and articular eminence. When a displaced disk returns to its normal position, it commonly produces a sound. However, it might also be noted that the disk does not recover its normal position, which is termed "no recapture." Disk derangement without recapture has been associated with worsening clinical and imaging changes over time. In some patients, the disk remains in a fixed position relative to the glenoid fossa and the articular eminence in both closed and open mouth positions. This is called "stuck disk" and is believed to be related to the formation of adhesions or fibrotic tissue. The retrodiskal layers are the most important attachments to be evaluated with MR imaging. The superior retrodiskal layer consists of elastic fibers, and the inferior retrodiskal layer consists of collagen fibers; they might be confused with the posterior band of the disk (pseudodisk sign). This occurs when a disk is displaced anteriorly and there is chronic thickening and fibrosis of the posterior attachments. Retrodiskal layer perforation may also be noted, which is overall more common than disk perforation. The other components of the retrodiskal tissue or "bilaminar zone" are neurovascular structures. Increased T2 signal in this region may be associated with painful joints and related to hypervascularity; however, decreased T2 signal might be associated with fibrotic changes in a chronic internal derangement.

As in most joints, narrowing of the space should be one of the first and most common findings to describe, particularly in the setting of degenerative osteoarthritis and chronic internal derangement. Joint effusion, capsular, or synovial abnormalities and loose bodies are also possible. Grading of joint effusions and clear parameters for pathologic effusions are not defined. Joint effusion is most commonly seen in symptomatic patients. However, it can also occur in asymptomatic volunteers, and its association with pain is controversial. When an effusion is seen in both sides of the joint (superior and inferior compartments), it is usually abnormal and should prompt the search for perforation of the disk or retrodiskal layers. The 2 compartments should not communicate, as the disk and its attachments separate them. Large effusions on both sides of the joint should raise suspicion for inflammatory arthritis. Sometimes, this might be difficult to differentiate from synovial proliferation. Gadolinium can help these patients by showing enhancement with synovial proliferation.

The capsule and synovium can be difficult to separate on MRI. In the postsurgical/arthroscopic setting, a thick and hypointense capsule can be easily depicted on gradient recalled echo (GRE) images. The synovium is usually altered in inflammatory arthritis. Minimal to no synovial enhancement is seen in a normal TMJ or in some patients with internal derangement or osteoarthritis. When present, synovial enhancement should raise suspicion for inflammatory arthritis such as rheumatoid, psoriatic arthritis and ankylosing spondylitis. Rheumatoid arthritis is characterized by both osseous

and soft tissue (synovial-pannus) involvement. As such, concomitant severe osseous changes in the condyle and enlarged synovium should allow differentiation of rheumatoid arthritis from severe degenerative osteoarthritis. In the latter, erosive bony changes are not accompanied by enlarged synovium. Gadolinium-enhanced MR imaging is particularly important for evaluating TMJ involvement in children with juvenile arthritis, in which case a delay in diagnosis could compromise normal facial growth.

Pigmented villonodular synovitis is a monoarticular disease of uncertain origin that can affect virtually any synovial joint. It is most common in the knee and hip. Rarely, the TMJ can also be affected, and early in the disease, imaging findings must be differentiated from those of inflammatory arthritis. PVNS is characterized by benign synovial proliferation. On MRI, an enlarging mass extending away from the joint with hemosiderin deposition is typical for PVNS. Synovial chondromatosis, another proliferative synovial disease, might be confused with PVNS. Both entities can cause mass-like enlargements of the joint. On MRI, hemosiderin deposition can be depicted as "blooming" on GRE or prominent hypointensity on T2-weighted images and is typical for PVNS, rather than synovial chondromatosis; however, loose bodies and joint effusion favor synovial chondromatosis. On CT, calcifications or calcific loose bodies would make the diagnosis of PVNS highly unlikely (PVNS virtually never calcifies), favoring synovial chondromatosis or perhaps CPPD.

Loose bodies in the joint can represent chondroid nodules, calcifications, or ossified fragments. Synovial chondromatosis (synovial chondromatosis) is a proliferative disorder associated with the formation of metaplastic cartilaginous or osteocartilaginous nodules in the synovial membrane that become pedunculated and eventually detach as loose bodies. Though the TMJ is infrequently affected by tumor or tumor-like conditions, synovial chondromatosis is the most common neoplastic lesion of the joint. Loose bodies, representing cartilaginous nodules, are characteristic of this disease. Given the fact that some nodules are not calcified, particularly during the early stages of the disease; MRI can have improved sensitivity over CT for their detection.

Calcifications within the joint are also seen with CPPD, mimicking the calcified cartilaginous nodules of synovial chondromatosis. Both CPPD and synovial chondromatosis, usually involve large joints such as the knee and rarely involve the TMJ. However, CPPD is not a neoplastic entity; it is, rather, an inflammatory type of arthritis characterized by deposition of calcium pyrophosphate dehydrate crystals in the hyaline cartilage, fibrocartilage, and other soft tissue structures. Epidemiologically, CPPD is more common in older persons (60 years of age), whereas synovial chondromatosis appears to have a predilection for the Asian population.

CPPD is characterized by 2 clinical patterns, an acute inflammatory attack (pseudogout) and tumoral calcium pyrophosphate deposition disease (tophaceous pseudogout). Tophaceous pseudogout (TCPPD) is the less common form of presentation. Interestingly, it seems to be the preferential form of presentation when CPPD occurs in the TMJ. TCPPD presents as a tumor-like condition with a cloud-like calcific appearance on CT, usually located circumferentially surrounding the condyle or in the anterior aspect of the joint. MRI features of TCPPD are rarely described in the literature. Chondroid metaplasia can be seen in pathologic specimens of CPPD. Thus, even on pathology, CPPD could be confused with synovial chondromatosis, pigmented villonodular synovitis, or chondrosarcoma. Although, the coexistence of synovial chondromatosis and CPPD has been previously reported, the hallmark for the diagnosis of CPPD is the presence of characteristic crystals on fine needle aspiration or pathology. In addition to the previously discussed entities of synovial chondromatosis and CPPD, the presence of a loose body can represent a bone fragment from osteochondritis dissecans, in which case, the donor site in the condyle can be identified.

CT is the preferred modality when evaluating bones, particularly in the setting of trauma. However, MRI can also demonstrate abnormalities of the condylar morphology and bone marrow and has the benefit of improved soft tissue contrast to evaluate any extra osseous extension of tumors. Flattening and osteophyte formation in the condyle should be recognized on MRI. Subcortical cysts can also be noted. These findings are common in advanced degenerative disease secondary to internal derangement. Though also associated with degenerative disease, the presence of cortical erosions should prompt a search for additional findings of inflammatory arthritis or infection. Degenerative osteoarthritis is considered a complication of internal derangement. However, the presence of osteoarthritis does not necessarily correlate with the degree of pain, as older patients with osteoarthritis of the TMJ may be completely asymptomatic.

Idiopathic condylar resorption, also known as "cheerleaders syndrome," is a poorly understood disease with isolated TMJ involvement in teenage girls. It is characterized by loss of condylar shape and volume in all 3 planes. Basically resorption of the subcondylar bone with preservation of the fibrocartilage is seen, probably caused by an estrogen-mediated exaggerated response to minor trauma. Condylar resorption can also occur in the setting of juvenile idiopathic arthritis (JIA) and should be included in the differential. However, on JIA, there is loss of the vertical height of the condyle with associated erosions and possible compromise of the fibrocartilage as

well as inflammatory findings on MRI such as synovial enhancement, fluid, bone marrow edema, and pannus.

Bone marrow abnormalities are better appreciated on T1 images. Decreased T1 signal representing bone marrow edema or sclerosis should be carefully evaluated. It can be seen in infection, osteonecrosis, or after radiation. Osteonecrosis in the TMJ differs from osteonecrosis in other bones, such as hip and shoulder. It is not associated with steroid use or sickle cell anemia, and its prognosis is better. On imaging, TMJ osteonecrosis can be challenging and demonstrates variable amounts of bone marrow edema and sclerosis.

The most common bone tumor in the TMJ is the osteochondroma. Bone cysts as well as primary or secondary malignant tumors of the bone are less frequent. Though unusual, other entities involving the bones such as fibrous dysplasia can also be seen.

The LPM affects the anterior translation of the condyle. Traditionally, the LPM has been divided in a superior and inferior belly. Recent research indicates that the muscle is constituted by one belly. However, its insertion to the TMJ is made by 2 components: superiorly, there is an identifiable tendon inserting through fibrocartilage, and inferiorly, the muscle attaches directly to the periosteum without a tendon. In addition, the fibers of the muscle and tendon may or may not attach to the anterior band of the disk (disk-capsular complex). Thickening of the LPM tendon at its insertion in the TMJ has been associated with disk derangement. It has been referred as the double disk sign. In the author's experience, visualization and grading of thickening of the LPM tendon is challenging.

Hypertrophy, atrophy, and contracture of the LPM are changes that can be recognized by MRI and are probably linked to internal derangement. In theory, in the early stages of disk derangement, spasm involving the muscle would demonstrate edematous changes. In later chronic stages, a component of fatty atrophy can be seen. However, patients with severe osteoarthritic changes can have normal images of the LPM and patients without temporomandibular disorders can have abnormal LPM findings. Occasionally, pathology of the adjacent masticator space can be the cause of TMJ symptoms. The masticator space might be involved by inflammatory/infectious conditions (usually odontogenic in origin) and benign or malignant tumors. Sarcomas are among the most common tumors of the masticator space. They can be confined by the masticator fascia and demonstrate a well-defined benign appearance. Thus, when a mass is identified in the masticator space, biopsy should be done promptly.

Given its multifactorial nature, the management of TMD should include a multidisciplinary team. Usually, therapy is performed in a stepwise manner with minimally invasive or invasive techniques, only considered after failure of conservative management. Conservative management includes occlusal splints, physical therapy, and pharmacotherapy (nonsteroidal anti-inflammatory drugs [NSAIDs] and muscle relaxants). Minimally invasive management includes intra-articular injections and arthrocentesis/arthroscopy with lavage and lysis. Invasive management includes arthroplasty (disk repositioning, disk repair, discectomy alone, discectomy with graft replacement, either by arthroscopic or open surgical approach) and total joint replacement. Total joint replacement is reserved for ankylosis or severely damaged joints that have failed all other more conservative treatment modalities. In other scenarios, controversy exists as to the ideal surgical treatment, and there is also variable success of disk repositioning. Generally, early stages of internal derangement can be treated with disk plication and repositioning, whereas late stages may be treated with discectomy with or without some form of interposition grafting. Although very few reports have compared different surgical modalities, arthroscopy has gained preference over open surgery, in part due to decreased complications and similar success rates.

Summarizing, the recognition of disk abnormalities or internal derangement is the most important step when interpreting TMJ images. A systematic approach to include the most important anatomic components of the joint and its dynamic is necessary. Although TMD is considered a multifactorial disease and management decision requires a multidisciplinary approach, it is important to recognize that imaging findings are paramount in their evaluation. Generally, CT and MRI should be viewed as complementary techniques with MRI being the choice for evaluation of the intra-articular components (internal derangement) and particularly important in patients in whom an infectious or inflammatory process is suspected. Finally, recognition and awareness of less common but important entities will help in the interpretation of TMJ imaging studies. The article is a comprehensive review of imaging that covers many topics in detail. The article would be a good reference for practitioners looking to learn more about TMJ imaging.

Tallat et al[200] devised a study to compare CBCT findings as well as the measurement of the joint space in TMD participants with non-TMD participants, discriminating between the incidences of these findings in different diagnostic groups, and to correlate these findings with the clinical diagnosis. The study was conducted in patients attending the TMJ and facial pain clinic at University Dental Hospital Sharjah, United Arab Emirates, between September 2011 and April 2014. CBCT images and clinical records of non-TMD patients who sought treatment at the hospital for purposed other than TMD were used retrospectively as controls. Patients were excluded from the study if they had received

previous surgical treatment or had limited mouth opening caused by only muscle pain or muscle spasm. The inclusion criteria were diagnosis of TMJ osteoarthritis or closed lock according to the Research Diagnostic Criteria for TMDs group IIb, IIc, and III. Inclusion criteria for the control group were ≥16 years of age with no pain related to their TMJ area or muscles of mastication, no limitation of movement or function of their TMJ, and no joint sounds. The diagnosis of TMD was confirmed by the history of signs and symptoms, clinical examination, and radiographic examination, including MRI.

Cone-beam computerized tomography examination was done for all TMD participants and compared with CBCT records of the control group. Exposure parameters were identical for all participants, as follows: tube voltage: 85 kV; radiation time: 3 seconds; tube current: 7 mA; effective dose: 75 mSv; voxel size: 150 mm (screen resolution 1366×768); and slice thickness: 1.0 mm. The same CBCT exposure protocol was followed for all participants. Image interpretation and measurements were done by the oral and maxillofacial surgeon and the oral radiologist. The results used in this study were those in which there was agreement between the authors.

The right and left TMJ areas were closely studied from the medial pole to the lateral pole of each joint in three planes: sagittal, coronal, and axial, noting the following radiographic criteria: flattening, or loss of an even convexity or concavity of the joint outlines, osteophyte; local outgrowth of bone arising from a mineralized joint surface, Ely cyst (sub cortical cyst); rounded radiolucent area that may be just below the cortical plate or deep in trabecular bone, condylar surface irregularity where the surface affected was specified, the distance from the deepest point on the concavity of the glenoid fossa to the highest point on the condyle in sagittal and coronal views and where the mean of the last 2 readings was recorded for joint space measurement.

On the coronal view, the image of the condyle on its widest mediolateral diameter was chosen as the reference view for reconstruction of the sagittal slices. In this slice image, a vertical measurement line was dropped from the deepest concavity of the glenoid fossa to the most superior surface of the condylar process. Another measurement line was drawn in the reconstructed sagittal image; the line was again dropped from deepest concavity of glenoid fossa to the most superior surface of the condylar process in a sagittal section of the condyle.

In terms of statistical analysis, the data analysis was performed using SPSS v16.0 software. The null hypothesis of equal proportions among individuals with TMD, osteoarthritis, and closed lock for each one of the conditions (surface irregularity, osteophytes, flattening, and cyst) were tested using Fisher exact test. The null hypothesis of equal values among individuals with TMD, osteoarthritis, and closed lock for the joint space was tested using the Student *t* test. The null hypothesis of equal proportion was rejected if *P* was ≤.05. The correlation coefficient test was used to examine the relationship between TMD and the other conditions.

The results included a total of 89 participants (56 women and 33 men) in the study, 34 ±21 mean years of age. According to the Research Diagnostic Criteria for TMDs group IIb, IIc, and III, participants were classified as non-TMD (43 participants) and TMD (46 participants) groups, whereas the TMD group was further divided into 2 subgroups, osteoarthritis (n=20) and closed lock (n=26) participants.

Assessment of the CBCT of both non-TMD joints and TMD joints showed a statistically significant difference between irregularities of the superior surface of the condyle in TMD joints, 41.3% (n=38), and in non-TMD joints, 15.12% (n=13), (*P*=.001), osteophytes, which were seen in 19.57% of the TMD joints (n=18) and in 1.16% of the non-TMD (n=1) (*P*<.001), and flattening of the condylar surface, which was seen more in the TMD joints, 17.39% (n=16) than non-TMD joints, 4.65% (n=4) (*P*=.024).

On comparing the non-TMD joints with the osteoarthritic joints, a statistically significant difference was found between the irregularities of the superior surface of the condyle in the osteoarthritic joints, 80% (n=32) and in the non-TMD joints, 15.12% (n=13) (*P*<.001). Osteophytes were found in 40% (n=16) of the osteoarthritic joints and in 1.16% (n=1) of the non-TMD joints (*P*<.001) and flattening of the condylar surface was found in 30% (n=12) of the osteoarthritic joints and in 4.65% (n=4) of the non-TMD joints (*P*=.003). No statistically significant differences were found on comparing the non-TMD and closed lock joints.

Assessment of the CBCT findings of osteoarthritic and closed lock joints showed superior surface irregularities in 80% of osteoarthritic joints (n=32) and in 11.54% of the closed lock joints (n=6), where the difference was statistically significant (*P*<.001). Osteophytes were seen in 40% of osteoarthritic joints (n=16) and in 3.85% of closed lock joints (n=2) where the difference was statistically significant (*P*=.006).

Measurements showed that participants with no TMD have significantly more joint space (5.64 ±1.88 mm) compared with those with osteoarthritis (4.57 ±1.97 mm) (*P*=.025). A Pearson product–moment correlation showed a positive correlation between TMD, osteophytes, and flattening of the condylar surface, which was statistically significant (r=0.331, *P*<.001).

Temporomandibular disorder is the most common cause of non-infective and non-dental pain in the orofacial region. The cause of TMD is regarded as multifactorial, but the relative importance of the individual factors is still unclear. Common physiological characteristics of this

entity are muscular pathology and/or joint pathology, for example, internal disk derangement and osteoarthrosis, which are not always painful. Successful management of TMD depends greatly on the accurate diagnosis of the present TMJ pathology. Clinical and radiographic evaluations are usually used simultaneously during the diagnostic procedure. Various imaging modalities have been used for evaluating the morphological bony changes of the TMJ.

Panoramic radiography, conventional tomography, and CT are used to judge the bony components of the joints, while MRI is used to judge the soft tissue components. Conventional linear or complex motion tomography underestimates small bone abnormalities, and the diagnostic accuracy of TMD is limited, although it is superior to panoramic radiographs in sensitivity and specificity for detecting osseous changes. Panoramic radiographs can provide a general impression of the joint, but they have low sensitivity in evaluating changes in the condyle due to structural distortion, superimposition from the zygomatic process, and the inability to show the entire articular surface of the TMJ. CT has high cost and relatively high radiation dosage, as well as a low access to equipment, which limits its use for evaluation of the TMJ.

Cone-beam computerized tomography has several advantages over CT, such as lower cost, better access to equipment, lower radiation, and diagnostic efficacy as high as CT, but superior to those of panoramic radiography and linear tomography. CBCT is also superior to CT for analyzing lateral slices in isolation, and combining coronal and lateral slices and has high dimensional accuracy in measuring facial structures. MRI remains the gold standard for imaging the intra-articular soft tissue components of the TMJ. CBCT provided an alternate method of cross-section image production to CT using a comparatively less expensive radiation detector than conventional CT.

TMD clinical evaluation was done using the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) diagnostic algorithms and then was compared and correlated with CBCT findings. The authors used plain CBCT to detect bony changes in patients with closed lock, osteoarthritis, as well as in controls (non-TMD). Diagnosis was confirmed using MRI. It has been reported that considering the cause of osteoarthritis, chronic disk displacement is one of the common causes, and reduced joint space is a common finding. It has been found that in arthritis of the TMJ, the head of the condyle is more frequently affected, followed by the articular fossa where the most common radiographic signs are erosion and condylar flattening. The authors compared the bony changes and joint space in both normal and TMD joints. Temporomandibular disorder joints were further subdivided into osteoarthritic and closed lock joints. Bony changes studied included flattening of the joint outlines, osteophyte, Ely cyst (subcortical cyst), and condylar surface irregularity where the surface affected was specified. Osteophytes and flattening of the condylar surface were found as the most common features of TMD. On comparing non-TMD with TMD joints, as well as with osteoarthritic joints, a statistically significant difference was seen among irregularities of the superior surface of the condyle, osteophytes, and flattening of the articular surfaces. On comparing non-TMD with closed lock joints, no statistically significant difference was seen among any of the studied criteria. On comparing osteoarthritic and closed lock joints, a statistically significant difference was seen between irregularities of the superior surface of the condyle and osteophytes. The results of the present study showed that CBCT findings are significantly associated with the clinical diagnosis of TMD. Osteophytes and flattening of the condylar surface are common features of TMD.

This article correctly notes that many of the osseous changes seen on a regular basis are due to the lack of disk coverage of the condyle. This article articulately describes the relationships between different types of osseous changes in the TM joint.

Wang et al[201] authored an article discussing the current understanding of pathogenesis and treatment of TMJ osteoarthritis. Osteoarthritis is described as a degenerative disease that is characterized by progressive cartilage degradation, subchondral bone remodeling, synovitis, and chronic pain. Patients with TMJ osteoarthritis usually have pain and dysfunction of the TMJ with reduced quality of life. The clinical diagnosis of TMJ osteoarthritis is mainly based on the radiographic features of the condyle and articular eminence, including erosive resorption, sclerosis, attrition, osteophyte formation, and cyst-like changes. Treatment of TMJ osteoarthritis is directed at relieving pain, decelerating the progress of the disease, and restoring TMJ function. The pain of patients with TMJ osteoarthritis can be mostly managed effectively with NSAIDs or arthrocentesis.

The first part of the article discusses many concepts regarding the pathogenesis of TMJ osteoarthritis beginning with inflammation. They classify TMJ osteoarthritis as a "low-inflammatory arthritic condition," as opposed to rheumatoid arthritis, which is classified as a high-inflammatory condition. However, considerable attention has been on the importance of inflammation in the progression of TMJ osteoarthritis. Their concepts are based on a rodent study showing an increased expression of IL-1β and TNF-α with experimental chronic inflammation of the TMJs. This theory is based on the decreased biomechanical property of the disk and implies that chronic inflammation in the TMJ deteriorates the adaptive capacity of the TMJ. They also discuss the role of excessive mechanical stress, the role of subchondral bone

in the initiation or progression of TMJ osteoarthritis, chondrocyte apoptosis and its role in the degeneration of osteoarthritic cartilage, the upregulation of catabolic enzymes, and the roles of estrogen and genetics.

The second part of the article discusses the treatment options for TMJ osteoarthritis. TMJ osteoarthritis therapy aims primarily to relieve symptoms, stop the disease progress, and restore TMJ function. The conventional treatment for TMJ osteoarthritis includes mainly nonsurgical options, such as physical therapies, occlusal splints, NSAIDs, and arthrocentesis with lubrication or corticosteroids. In regard to occlusal splints, the authors provide a detailed discussion of a stabilization splint that is effective in inducing favorable condylar bone remodeling for patients with TMJ osteoarthritis. Treatment of TMJ osteoarthritis should be directed at eliminating preexisting risk factors. A stabilization splint may be more suitable for the patients with TMJ osteoarthritis with evident muscle overuse or severe bruxism.

Surgery is discussed as the last recommendation for the treatment of TMJ osteoarthritis. Surgical intervention, such as joint replacement with autologous bone or an artificial joint, may restore joint function to some extent in patients with severe impaired joint function and intractable pain. However, joint replacement does not fully restore the destroyed organ, and the long-term prognosis is uncertain, with some patients requiring a second operation. Most of the treatments are effective in terms of decreasing pain, and some treatments decelerate joint degeneration; however, treatment rarely restores the destroyed joint. Lastly, they comment on options such as cytokine-based therapy, NSAID therapy, visco supplementation, and regenerative medicine.

This article is based on the concept that chronic inflammation may be the initiating factor in TMJ osteoarthritis. There was minimal discussion of the disk and the role it plays in maintaining the integrity of the mandibular condyle. This article also was primarily an animal study review with many questionable assumptions regarding the human TMJ based upon various animal studies. The assumptions appear to support a theory that is not supported clinically or in the literature, given the multiples articles published outlining condylar changes that occur after the displacement of TM disk.

The final imaging article review was by Larheim et al,[202] who published a paper discussing TMJ diagnostics using CBCT. They discussed the diagnostic accuracy and show CBCT, generally has an acceptable accuracy for diagnosing osseous TMJ abnormalities with fairly high sensitivity, although small abnormalities may be missed. However, there are differences between different CBCT scanners and imaging protocols. In most studies, high specificity is reported. The diagnostic accuracy of CBCT seems to be comparable with that of CT for TMJ diagnosis. Observer variation has been studied by several authors and generally seems to be acceptable. The observer agreement may be higher with smaller fields of view, and observers are also influenced by the size of bone defects. The smaller the defect, the more difficult is its identification, with a lower percentage of observer agreement.

Although the literature for TMJ diagnostics using CBCT has become rather extensive, the current available data seem to be limited to the first 2 levels in the 6-stage framework to assess the efficacy of imaging methods: technical efficacy and diagnostic accuracy efficacy. Little attention has been paid to the next 2 levels of the 6-stage framework: diagnostic thinking efficacy and therapeutic efficacy. This is particularly important in evaluating patients with TMD, those being the largest group of patients undergoing TMJ imaging procedures. To the best of the author's knowledge, only 1 study has focused on the value of CBCT examinations in clinical decision making, primary diagnosis and management of patients with TMD. The clinical decision changed in more than half of the patients when based on physical, panoramic, and CBCT examinations compared with a decision based only on physical and panoramic examinations. Thus, the usefulness of CBCT in patient management was clearly demonstrated.

In a relatively short period of time, CBCT has emerged as a cost-and dose-effective alternative to CT for examination of TMJ disorders, although it may be more sensitive to motion artifacts. The imaging modality is superior to conventional radiographic methods, as well as MRI, in the assessment of osseous TMJ abnormalities. However, the diagnostic information obtained is limited to the morphology of the osseous joint components, cortical bone integrity, and subcortical osseous abnormalities. For the assessment of inflammatory activity and soft-tissue abnormalities such as internal derangement in patients with TMD, MRI is the method of choice. Knowledge about the impact of CBCT examinations on patient outcome is lacking and research in this area is needed. This article points out the importance of understanding the anatomy of the TM joints and how it relates to treatment recommendations for each specific patient. The ability to understand the condition of the hard tissues through CBCT and soft tissues through MRI allows dentists to have a more informed discussion with patients regarding treatment options.

Although most TMJ imaging studies evaluate the condyle of the disk, de Castro Lopes et al[203] designed a small study of 20 patients to compare the volume of the lateral pterygoid muscle in patients with migraine with that in a control group of volunteers without migraine by using the segmentation of the lateral pterygoid muscle and MRI images of the TM joint to determine the volume of

the lateral pterygoid muscle. The study sample consisted of 20 patients with migraine (8 men and 12 women; 21 to 49 years of age; mean 39.3 years) and the control group consisting of 20 volunteers without migraine or any signs or symptoms of TMDs (10 men and 10 women, 18 to 75 years of age; mean 42.4 years). Migraine was diagnosed and patents were selected by an expert neurologist. Patients with no symptoms of migraine according to the international classification were excluded from the patient group. Both the control and patient groups underwent a clinical examination of the TMJ conducted by an experienced orofacial pain specialist according to the Research Diagnostic Criteria for TMDs.

MR imaging was performed on all patients and controls using a 1.5-T MR imager with a bilateral and dedicated circular polarized 8.0-cm transmit-and-receive TMJ coil. Images were obtained in closed-mouth and open-mouth positions. Using the axial localizer image, parasagittal images (perpendicular to the condylar axis) were obtained and selected to analyze the disk-condyle relationship. Statistically significant differences between the 2 groups were found for all the variables analyzed. This was confirmed by the chi-squared and Fisher exact tests (α=.05). Disk displacement, absence of disk reduction, abnormal condyle motion, joint noise, articular and/or muscle pain, and limited mandibular range of motion were found more frequently in the migraine group than in the control group. With regard to the volume of the LPM, the Student *t* test showed a statistically significant relationship between migraine and increase of LPM volume. According to logistic binary regression, the relevant factors that predicted the presence of migraine headache were limited mandibular motion (relevance 61.2%), increased volume of the LPM (relevance 58.7%), and disc displacement (70.0%).

This study showed that the LPM tends to be hypertrophic in patients with TMDs and simultaneous migraine. Furthermore, disk displacement and abnormal mandibular movements seem to be the most common signs in patients with migraine and TMDs. Although not all patients with TMDs and migraine showed LPM hypertrophy, these results suggest that TMDs can be a cause of LPM hypertrophy. Moreover, the results suggest that the known difficulties in using palpation alone to study the LPM may be circumvented by using LPM segmentation on MR imaging as an alternative method for studying this muscle.

TM joint imaging has become part of the protocol for diagnosing TMJ condition. In addition to imaging, articulator-mounted study casts also play a role in the diagnosis and treatment planning for occlusion, restorative treatment, and patients with TMDs. Lux et al[204] used 15 dried human skulls to evaluate maxillary cast mounted using the Kois Dento-Facial Analyzer with cast mounted from using Panadent Pana-mount facebow (facebow). Fifteen dried human skulls were used. Lateral cephalometric radiographs and 2 maxillary impressions were made of each skull. One cast from each skull was mounted on an articulator by means of the analyzer and the other by using the facebow. A standardized photograph of each articulation was made, and the distance from the articular center to the incisal edge position and the occlusal plane angle were measured. The distance from condylar center to the incisal edge and the occlusal plane angle were measured from cephalometric radiographs. Finally, the 3D position of each articulation was determined with a Panadent CPI-III. A randomized complete block design analysis of variance (RCBD) and post hoc tests (Tukey-Kramer HSD test) (α=.05) were used to evaluate the occlusal plane angle and axis-central incisor distance. A paired 2-sample t test for means (α=.05) was used to compare the X, Y, and Z distance at the right and left condyle.

The analyzer and facebow mounted the maxillary cast in a position that was not statistically different from the skull for comparing the occlusal plane angle (P=.165). Both the analyzer and the facebow located the maxillary central incisor edge position in a significantly different position compared with that of the skull (P=.001) but were not significantly different from each other. The 3D location of the maxillary casts varied at the condyles by approximately 9 to 10.3 mm.

The analyzer mounted the maxillary cast in a position that was not statistically different from the facebow when comparing the incisal edge position and the occlusal plane angle. Both the analyzer and the facebow located the maxillary incisal edge position in a significantly different position compared with the anatomic position on dried human skulls.

With the increase in digital impression scanning, new techniques must be developed to maximize the capability of the technology. Solaberrieta et al[205] present a protocol that describes a method of virtually locating the digital casts onto a virtual articulator by means of an intraoral scanner, a digital camera, and software (Agisoft and reverse engineering software). The facebow and centric relation record have long been used to orient dental casts on an articulator in the same relationship as that in the patient's mouth. However, the shift to the virtual environment has only just begun in terms of the facebow, and standard methodologies need to be developed and tested before the virtual facebow is part of routine practice. This virtual facebow was developed to locate the maxillary digital cast of the patient in a cranial coordinate system. The present protocol also allows the dentist to locate the mandibular digital cast exactly on the maxillary digital cast by using the virtual interocclusal record.

Several CAD-CAM system provide a virtual articulator simulation. The first virtual articulator was based on

a mathematical simulation of the mandibular movements that take place in an articulator and was designed to record the exact movement paths of the mandible by using an electronic jaw movement registration system called Jaw Motion Analyser (Zebris) and then to move digitized dental arches along those paths in the computer. With these tools, static and kinematic occlusal collisions could be calculated and visualized. However, the main problem with those virtual articulators was transferring data from the patient to the simulation. The technique presented here overcomes this the virtual facebow is part of routine practice. The present protocol also allows the dentist to locate the mandibular digital cast exactly on the maxillary digital cast by using the virtual interocclusal record.

Phase 1: obtaining photographs and transferring data

1. Scan the maxillary and mandibular dental arches of the patient with an intraoral dental scanner to obtain digital casts.
2. Place 3 adhesive targets onto the patient's head. Locate the first 2 points next to the temporomandibular joints and the third point onto the infraorbital point.
3. Locate irreversible hydrocolloid or scannable elastomeric impression material on a plastic, colored facebow fork and introduce the facebow fork into the patient's mouth, pushing it against the maxillary arch.
4. Make 8 to 10 photographs by using a digital camera (minimum of 5 MB and constant values for minimum ISO [exposure index] setting, lens F value, and no flash) and reverse engineering software to obtain the 3D spatial relationship of the shape of the head with target points related to the facebow. Load the images into the software and build the 3D geometry of the patient's face with targets positioned on the facebow fork.
5. Scan the impression and the front side of the facebow fork with an intraoral dental scanner
6. Using reverse engineering software and load the facebow fork 3D geometry and align it to the maxillary digital cast by using the best-fit command you look at what you.
7. Repeat step 6 of this protocol, aligning the 3D face-facebow fork and impression-facebow fork

Phase 2: alignment of 3D face-facebow fork and impression-facebow fork

8. Blend the different surfaces of the scanned maxillary digital cast into a single virtual cast, eliminate surface abnormalities, remesh the organization of the triangulated mesh of points, and fill in the surface gaps that remain after data elaboration.
9. Create the cranial coordinate system by using the 2 temporomandibular points and the infraorbital point, locating the maxillary digital cast on this reference system.
10. Transfer the maxillary digital cast to the virtual articulator software, bringing the cranial coordinate system to coincidence with the virtual articulator's coordinate system.
11. Locate the mandibular digital cast, scanning the virtual interocclusal record with an intraoral scanner in centric occlusion from 3 directions (left, right, and front). Match these scans with the maxillary and mandibular digital casts, positioning the mandibular digital cast towards the maxillary digital cast in the virtual articulator in maximum intercuspation.

The primary advantage of this technique is that it works with any type of virtual articulator, thus generating a universal virtual facebow. Because the procedure results in a dental digital database, patient information can be transferred to any machining or sintering center in the world, resulting in greater flexibility and autonomy. In addition, this technique provides a digital copy of the patient's face that is available throughout the diagnostic, planning, and treatment phases.

Diagnostic study casts are necessary to fabricate occlusal appliances which are one of the most common treatment modalities for muscle problems for TMJ patients. Aksakalli et al[206] compared the efficacy of stabilizations splints and NTI appliances. A total of 40 patients (34 women and 6 men, mean 31 years of age) with TMD were included in this study. Group SS consisted of patients using a stabilization splint. Group NTI consisted of patients using the NTI. There were 20 patients in each group. Impressions and centric relation records in wax were made of all patients. The SS were made in heat-polymerized acrylic resins by 1 technician. The NTI splints were made. The SS were fabricated to provide separation of the posterior teeth during protrusion and canine rise during lateral excursion. These splints were adjusted to permit freedom of movement between the condyle disk and articular eminence in the centric relationship and to include multiple bilateral occlusal contacts in the contact position of maxillary and mandibular teeth when the mandible is retruded. NTI were prepared according to the manufacturer's instructions and adjusted chairside.

Within the limitations of the study, the following conclusions can be drawn. First, over the long term, the patients in both groups (SS and NTI) reported fewer TMD complaints, but group NTI revealed no statistically significant difference in that regard. Second, following

splint therapy, patients with TMD experienced less difficulty moving the mandible from side to side, less trouble opening the mouth and fewer complaints of being nervous. Third, the major complaint of patients with TMD was clenching and grinding, followed by pain in the craniomandibular joint or earache. Last, both splints reduced the patients' amount of pain over the 3-month observation period. This main limitation in the study is the lack of imaging to assess the condition of the tissues the occlusal appliances were being used to treat. A common question regarding occlusal splints relates to the changes in vertical dimension that occur with the use of occlusal appliances.

Moreno-Hay and Okeson[113] authored a literature review regarding the effect of altering the occlusal vertical dimension on producing TMD symptoms. The authors conducted a comprehensive search through PubMed from 1966 to 2013 with the following search MeSH terms "temporomandibular disorders," "occlusal vertical dimension," "stomatognatic system," "masticatory muscles," and "skeletal muscle." Filters for English language were applied. A total of 380 were initially identified. After reading the abstracts, only 71 papers were selected. After full-text analysis, 6 papers were excluded as not having information related to this subject review. Bibliographies of all retrieved articles were consulted for additional publications, and 2 additional articles were disclosed. Hand-searched publications from 1938 were included. A total of 67 papers met the purpose of the study. These papers were reviewed, and both authors concluded that there were no randomized clinical trials available. The articles were often scientifically flawed because of design flaws, small study populations, lack of controls, and others. Furthermore, most of the conclusions were based in case reports and opinions rather than in well-controlled clinical trials. This article will review the past and present views, and the authors will compare the clinical opinions on this topic and the outcomes reported in the available literature.

A review of the available literature regarding the effect of increasing occlusal vertical dimension (OVD) is limited. The scientific merit of the available studies is compromised by the lack of adequate sample size, control groups, randomization and, in most of the patients, long-term follow-up. However, in spite of these shortcomings, the results of these studies do not suggest that increasing the OVD leads to the development, aggravation or perpetuation of TMD symptoms. On the contrary, the few published studies show a trend demonstrating that mild transient TMD symptoms may appear after moderate increases of OVD and these symptoms routinely resolve rather quickly. These findings suggest that the stomatognatic system has great ability to adapt to increases in OVD without any major clinical consequences.

A review of the available literature regarding the effect of decreasing OVD on producing TMD is very limited. There are no well-controlled studies, and most opinions are drawn from observations associated with loss of tooth structure. A decrease in OVD may occur with the loss of posterior teeth but, because other risk factors such as occlusal instability are involved, the relationship between decreased in OVD and TMD cannot be determined. It is logical to assume that a severely worn dentition results in a decrease in OVD. However, evidence does not suggest that there is increased presence of TMD symptoms in severely worn dentition. Perhaps this is further evidence of the favorable adaptability of the stomatognatic system.

Much of the concepts regarding OVD and TMD are unfounded by scientific evidence. Additional studies are needed to more completely understand this relationship as well as important factors that may need to be considered when there are clinical needs to change a patient's OVD. This article points out that some of the long standing beliefs in restorative dentistry may require modification. A new perspective on vertical dimension could evaluate the changes in TM joint dimension and how dimensional changes in the TM joint impact the facial skeleton.

Manfredini et al[207] addressed this topic and made a systematic review of the literature on the relation between facial skeletal structures and temporomandibular joint disorders. Although the literature on the relation between TMD and occlusion has been reviewed previously, studies on the association with different facial morphologies have never been summarized systematically. The potential existence of a skeletal predisposition to TMDs has been suggested in a recent hypothesis postulating that, for the occurrence of disease, there is a need for an imbalance between the load exerted on the joints and their capability of bearing the load.

On June 30, 2014, a systematic search of the dental and medical literature was performed to identify all peer-reviewed articles in the English language dealing with the relation of facial morphology to TMDs published during the past 30 years. The systematic review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The combination of different search keywords in the Medline database identified 92 potentially relevant citations, 45 of which were retrieved in full text after reading the abstract. The search expansion strategy allowed an additional 9 full texts for consideration. Based on the reading of the full text, 12 articles were excluded for not fulfilling the inclusion criteria and 8 articles for redundancy, thus accounting for a total of 34 articles included in the review. For discussion purposes, the reviewed articles were grouped based on the targeted age class of the study population (adolescents or adults based on whether patients were teenagers at the end of the study) and of

the TMD under investigation, namely disk displacement (adolescents, n=4; adults, n=16), osteoarthritis or osteoarthrosis (adolescents, n=0; adults, n=8), or unspecified TMD signs and symptoms (adolescents, n=3; adults n=3).

The report reviewed the available literature on the relation between facial morphology and TMDs. As a general remark, the quality of the available literature is questionable. Indeed, even in the absence of threshold scores for the Newcastle-Ottawa Scale instrument, quality assessment showed some recurrent methodologic flaws. Importantly, the populations chosen for each study were quite heterogeneous (such as, patients with orthodontics, patients with TMD, and patients with malocclusions), and not all studies included a true control group. As a consequence of the variable selection process for the study populations, the percentage of patients with TMD differed among the various investigations. Moreover, the number of studies determined for the comparable category was smaller, especially for the very few research groups that were involved. Based on these factors, this review's suggestions are based more on the reviewers' attempt to find a common theme among such miscellaneous findings than on evidence-based data.

The adolescent studies reviewed the relation between facial morphology and disk displacement and the relation between facial morphology and TMD signs and symptoms. The adult studies reviewed the relation between facial morphology and disc displacement, the relation between facial morphology and TMD signs and symptoms, and the relation between facial morphology and TMJ osteoarthritis or osteoarthrosis.

The findings suggest that disk displacement or degenerative joint disease was associated with a decreased growth of the mandible in the adolescent and adult samples. Skeletal features associated with TMDs included short ramus height and mandibular length, a steep mandibular plane angle, and an increased profile convexity and retrognathism. Facial asymmetry also was associated with unilateral or bilateral pathology of greater severity on the ipsilateral side.

The association between TMDs and facial morphology in adults was assessed mainly by comparing the prevalence of imaging detected abnormalities and clinical signs and symptoms in patients with different skeletal features. Such a study design did not allow the determination of which condition occurred first (the skeletal morphology or the TMD) and whether the 2 conditions were causally related. In theory, these 2 hypotheses are plausible. For instance, several investigators have suggested an etiologic role of TMJ internal derangement in the abnormal development of the facial skeleton based on the concept that the condyle represents an important growth site within the craniofacial skeleton. According to this view, disk displacement can be seen as a localized disturbance in the functional environment of the TMJ, thus accounting for compressive stress and decreased lubrication of the joint surfaces with inflammation and tissue damage, ultimately resulting in a condylar and ramus height reduction.

Animal experiments also have found that disk displacement occurring during the developmental period induces impairment of mandibular growth. Conversely, the genetically determined or acquired skeletal deformity could contribute to the onset of disorders within the TMJ because of the increased susceptibility to microtrauma or macrotrauma to the joint system.

Studies of growing patients should have been more suitable to investigate these hypotheses, but, unfortunately, most studies were cross-sectional and did not provide any cause-and-effect information. The reviewed literature on adolescent samples supports in part the association of TMJ disk displacement with a shorter posterior facial height, a shorter mandibular length, clockwise rotation, and retruded mandible position, namely a skeletal Class II profile with shorter mandibular corpus and ramus. Interestingly, findings from adolescent studies dealing with the presence of clinical TMD signs and symptoms did not support their association with any specific growth patterns, possibly suggesting that such younger asymptomatic patients might develop clinical TMD symptoms later in life as a result of the progressive loss of their TMJs' adaptive capacity.

In summary, studies on adults and adolescents suggest that short ramus and posterior facial height and the backward position and rotation of the mandible are the main features associated with TMJ disc displacement. Those features are common to skeletal Class II and hyperdivergent growth patterns. The same skeletal features also related positively to the progression of degenerative joint disease or TMD signs and symptoms in adults.

Based on these observations, patients with skeletal Class II and hyperdivergent facial patterns might be more prone to TMDs. A possible explanation for such findings can be found in the literature describing that such joints are characterized by poor reciprocal fitting of the articular surfaces (small condyle and wide glenoid fossa), and they are potentially at risk of developing disk position abnormalities because of joint instability. Conversely, patients with skeletal Class III and hypo-divergent patterns might be less predisposed to TMJ disk displacement because of their biomechanical advantage.

Based on this systematic literature review on the possible associations between TMDs and facial morphology, the following suggestions can be drawn. First, the quality of the available literature is not adequate to provide an evidence base on the topic. Second, despite the heterogeneity of design and findings of the reviewed

articles, it seems reasonable to suggest that skeletal Class II profiles and hyperdivergent growth pattern are likely associated with an increased frequency of TMJ disk displacement and degenerative disorders. Third, prospective cohort studies are needed to assess the actual existence of a causal link.

This article summarizes many of the clinical observations commonly seen with Class II patients. A key point noted in the article is that Class II profiles and hyperdivergent growth patterns are likely associated with changes in the TMJ.

Related to class II occlusions, Tinastepe and Oral[208] published an article comparing the TMD and psychopathology in patients with increased vertical overlaps between maxillary and mandibular incisors (vertical overlap 4 mm) and control groups according to the RDC/TMD in adult dental patients. The aim of this study was to test the null hypothesis that there is no association between increased vertical overlap with minimal horizontal overlap (horizontal overlap of 2 mm) and signs of TMD. Furthermore, this study proposed to investigate any correlation between TMD and patient psychopathology.

The selection criteria for this group were presence of increased vertical overlap (vertical overlap 4 mm), presence of minimal horizontal overlap (approximately 2 mm), and presence of tooth contacts in the anterior teeth (central and lateral incisors) in habitual occlusion. At least 2 contacts between maxillary and mandibular central and/or lateral incisors were required to prevent negative effects of tooth eruption due to periodontal reasons, among others. To measure vertical overlap, the level of the incisal edges of maxillary incisors was marked with a pencil on the labial surfaces of mandibular incisors. The distance between this reference line and the incisal edges of the mandibular incisors was measured with a millimeter ruler. The greatest incisor vertical overlap measurement was recorded as vertical overlap. The least horizontal distance, measured by a ruler, between the incisal edges of the maxillary incisors and the labial surfaces of the mandibular incisors was recorded as horizontal overlap. The selection criteria for the control group were the absence of any contacts between the anterior teeth (lateral and central incisors). Thus, horizontal movement of the mandible would not be prevented by the maxillary anterior teeth, as in patients with increased vertical overlap with minimal horizontal overlap.

This study found that some of the signs of TMD occurred more often in patients with increased vertical overlap anteriorly with minimal horizontal overlap than in control patients. Hence, the null hypothesis of the study, which stated that there was no association between increased vertical overlap and signs of TMD, was rejected. Statistically, in this study, no significant differences in depression or pain severity between the 2 groups. This study indicated that clinicians should pay special attention to the TMJ status of patients with increased vertical overlap anteriorly and position of the incisors when performing dental treatments that require reestablishment of the incisor relationship. This study reinforces the concept that structural changes in the TM joints can affect the occlusion and most notably in the anterior segment resulting in the uncoupling of the anterior teeth and a Class II occlusion.

Many growing Class II patients are treated with functional appliances. Al-Saleh et al[209] published a systematic review of the literature to evaluate the fixed mandibular reposition appliance's effects on TMJ morphology and position (condyle, glenoid fossa, and articular disk) in skeletal class II malocclusion treatment. Mandibular retrusion is considered the most common characteristic of class II malocclusion in children and adolescents. Mandibular repositioning appliances have been reported to successfully correct class II malocclusions. However, it is uncertain whether these appliances have beneficial or harmful effect on the articular tissues of the TMJ. It has been suggested that fixed repositioning appliances apply near constant forces to the TMJ and may cause remodeling of the articular condyle and glenoid fossa, repositioning of the condyle and rotation of the mandibular body, which may lead to permanent damage to the TMJ structures.

Four databases, (MEDLINE, EMBASE, All EBM Reviews, and Scopus) were systematically searched in every language. Keywords used in the search were "orthodontic appliances," "functional/activator appliances," "Crossbow," or "Forsus," or "Jasper Jumper," or "Herbst," or "MARA," or "Functional Mandibular Advancer," "temporomandibular joint," "TMJ," "temporomandibular joint disc," "jaw joint," "mandibular joint," "computed tomography," "cone-beam computed tomography," or "magnetic resonance imaging." A librarian specializing in health sciences databases was sought to identify the best selection of both truncated and MeSH terms.

Clinical trials, cohort studies, case-control studies, cross-sectional studies, prospective and retrospective studies that studied the TMJ morphologic and positional changes after non-surgical class II malocclusion treatment using fixed appliances were included. Case series/reports (unless consecutively treated), commentaries, editorials and letters were excluded. Inclusion was restricted to children and adolescent patients with skeletal class II malocclusion treated with fixed mandibular anterior repositioning appliance. Any changes of the TMJ articular tissues, assessed by 3D imaging modalities (MRI, CT, CBCT), were included.

The electronic database search yielded a total of 269 articles. The primary review resulted in 30 potential articles that were further considered for inclusion. Based on

a full-text review, 17 articles were selected. All included articles were considered to have high risk of bias. Multiple forms of bias were evident such as missing control group, ignoring sex effect as a co-factor, and inadequate measurement tools and data analysis. Ten articles did not conduct blinding during image analysis. Four articles report descriptive analysis without proper statistical analysis. One article reported results in graphics, which led to missing or unclear data. Significant methodological limitations were identified in all the included articles. The high risk of bias in considering sex as confounding variable, blinding, untreated control, and incomplete outcome reporting deemed the findings questionable.

Current literature that examined the short-term effect of fixed functional appliances on actively growing patients showed critical design problems and analytical flaws that prevented drawing any definite conclusions about conducted treatments. The articles failed to establish evidence of the TMJ tissue reaction to the forces applied by the mandibular anterior positioning appliances.

A well-designed study is required to establish articular tissue reactions to the mandibular anterior appliances to treat class II malocclusion in the adolescent population. Suggestions for future research design are as follows:

1. Although ethically questionable if not properly planned, a randomized clinical trial with untreated control is the ideal design to detect the causal effect on TMJ accurately.
2. A larger sample size to empower the collected data analysis and support the clinical significance of the reported findings.
3. Use 3D volumetric CBCT images before and after treatment with a standardized imaging protocol to overcome the shortcomings of the 2D images in evaluating the osseous changes of the TMJ. A valid and reliable superimposition technique should be conducted to quantify the osseous remolding.
4. Despite the implicit ability of MRI to render soft tissue contrast and high resolution, it is paramount to adequately evaluate the disk position in relation to the condyle and glenoid fossa using a valid and reliable tool adequately. Ideally, the articular disk should be segmented to avoid losing critical data and enhance the accuracy of the assessment process.
5. A double-blinded experienced examiner should conduct the image analysis to reduce method error and improve the assessment reliability.
6. Appropriate data analysis that considers age and sex should be performed to assess the evidence of the collected findings.

While functional appliances are one option to treat class II occlusions, another option is the use of orthognathic surgery. Nadershah and Mehra[210] wrote an article on orthognathic surgery in the presence of TMD and posed 6 questions regarding orthognathic surgery. The first questions is does malocclusion cause temporomandibular dysfunction? The literature reports a significant variation in prevalence of TMD in patients with skeletal malocclusion. Many studies report higher incidence of TMD in patients with retrognathic mandibles; these patients usually have steep occlusal and mandibular planes (high angle). Other studies report higher incidence in class III patients, most of whom have flat occlusal but steep, high mandibular planes (low angle). This finding is likely a reflection of the multifactorial causes of TMJ disease. In the authors' experience, they have noticed a higher incidence of TMD in patients with retrognathic mandibles and in those with steep occlusal planes, as mentioned earlier. Even so, most of the published literature in TMD incidence is limited by small sample sizes and selection bias.

The second question is what is the effect of orthognathic surgery on temporomandibular dysfunction? The two main philosophical approaches are that orthognathic surgery aids in the reduction of temporomandibular joint dysfunction or does not aggravate the current temporomandibular dysfunction as opposed to orthognathic surgery causing further deleterious effects on the temporomandibular joints. This is a difficult area to study and research because of multiple differences in the classification, diagnosis, and treatment of TMJ internal derangement. When the existing literature is critically evaluated, it becomes evident that the inferences are often based more on anecdotal opinion and clinician experience. Recommendations have been rationalized on less than optimal or flawed, retrospective, chart review–type research protocols. There are no randomized, prospective, multicenter clinical trials studying this complex relationship. If one were to pick a subgroup of patients who could possibly have adverse outcomes after orthognathic surgery relative to preexisting TMJ signs and symptoms, it is likely to be high-angle, class II patients undergoing counterclockwise rotation or large mandibular advancement procedures.

The third question is what is the effect of orthognathic surgery and mandibular range of motion? For most patients, orthognathic surgery should have no long-term beneficial or adverse effects relative to mandibular mobility. The maximum interincisal opening is expected to decrease in the immediate, short intervals after surgery in almost all patients, with a greater decrease in patients who are kept in maxillomandibular fixation postoperatively.

The fourth question is what is the effect of orthognathic surgery on the maximum occlusal force? The maximum occlusal force changes after orthognathic surgery are affected by multiple factors and cannot be solely explained based on mechanics. Despite variability in the

literature, multiple studies indicate that mandibular setback increases the occlusal force, and mandibular advancement did not improve the masticatory function.

The fifth question pertains to 2 different surgical orthognathic techniques and movements that have variable effects on temporomandibular dysfunction Existing literature is inconclusive relative to the superiority of an intraoral vertical ramus osteotomy (IVRO) or sagittal split osteotomy (SSO) for mandibular setback procedures. In our opinion, an experienced clinician can obtain stable results with either procedure. The choice should be based on factors like personal experience and patient preference. There is no substitute for sound surgical technique. Removing all bony interferences between the proximal and distal segments, passive seating of the condyles intraoperatively, and use of positional screws rather than compression or lag screws for fixation should minimize the displacement of the condyles after SSO. Miniplates are considered more forgiving than bicortical screws for SSO fixation as they permit condylar seating with lesser potential for torque and/or sag.

The sixth question is what is the effect of the rotation of the occlusal plane on the temporomandibular joints? With proper surgical technique, both clockwise rotation and counterclockwise rotation (rotation of the occlusal plane [MMC] are stable and predictable orthognathic surgical movements if the TMJs are able to withstand the postsurgical loading and stress. counterclockwise rotation MMC leads to greater loading on the TMJs compared with clockwise rotation MMC after double jaw orthognathic surgery. Sequencing of bimaxillary surgery plays a critical role in seating the condyles in bimaxillary surgery, especially when the occlusal plane is altered. The mandible-first approach may have multiple advantages, when large, complex movements are planned in patients with TMDs that may interfere with optimal and accurate pre-surgical record obtaining, perioperative treatment planning, or intraoperative surgical execution.

Combined surgical-orthodontic treatment via orthognathic surgery is a common and well-accepted management approach for patients with dentofacial deformity. It aims to produce more harmonious facial skeletal relationships, with an objective to prevent long-term deleterious effects on the TMJs and dentition. The improvement criteria of TMJ symptoms after orthognathic surgery are often based on lack of pain or clicking and popping of TMJ.

A precise evaluation of joint structures is of major importance in the diagnostic assessment of abnormalities, because clinical examination alone does not always provide a complete understanding of the changes in intra-articular anatomy. Thus, an accurate diagnostic assessment with MRI is indispensable. The importance of MRI in the diagnosis of TMD has been confirmed in numerous studies.

The classification system of the clinical diagnostic criteria for TMDs is not sufficiently reliable for determining TMJ, internal derangement, and osteoarthritis. A clinical diagnosis of may need to be supplemented by evidence from an MRI to determine functional disk-condyle relationship. This articles clearly emphasizes the need to understand the structural condition of the TM joint prior to orthognathic surgery in order to understand the risks for instability after the surgical procedure.

Moving from an orthodontic surgical perspective to a TMJ surgical perspective, Al-Moraissi[211] published a systematic review of the literature to assess the clinical outcomes of 3 surgical message for the management of internal derangement of the TMJs. The first with arthroscopic lysis and lavage (ALL), the second was arthroscopic surgery (AS), and the third was open joint surgery (OS). An electronic search of the PubMed, Ovid MEDLINE, and Cochrane CENTRAL on-line databases was conducted from their respective dates of inception to August, 2014. This systematic review and meta-analysis was conducted according to the PRISMA Equity 2012 checklist.

The following inclusion criteria were adopted in accordance with the PICOS criteria: Patients (P): those patients with internal derangement-like anchored disk phenomenon, disk displacement with or without reduction, painful click, and closed lock. Intervention (I): open surgery such as discectomy, meniscoplasty, local repair of perforation, high condylectomy, disk repositioning, and arthroplasty were the intervention in the OS versus AS comparison; electrocautery of the pterygoid ligament, myotomy of the lateral pterygoid muscle (or both), motor debridement, and disk suturing were the interventions in the ALL versus AS comparison. Comparator (C): this was arthroscopic surgery in the OS versus AS comparison and arthroscopic lysis and lavage in the ALL versus AS comparison. Impairment (C), and postoperative clinical findings (clicking, joint tenderness, and crepitation). Study design (S): human studies published in English, including randomized (RCTs), quasirandomized controlled clinical trials, controlled clinical trials (CCTs), and retrospective studies whose aim was to compare open surgery to arthroscopic surgery for the management of internal derangement of the TMJ. Outcomes (O): pain by VAS, maximum inter-incisor opening (MIO), mandibular function. The following were excluded: case reports, technical reports, animal or in vitro studies, review papers, and non-controlled clinical studies.

The electronic search resulted in 802 articles. Of these 802 articles, 301 were excluded because they were retrieved in more than 1 search. After the initial screening of the titles and abstracts, 323 articles were excluded because they were off-topic. Assessment of the full-text reports of the remaining 178 articles led to the exclusion of 171 because they did not meet the

inclusion criteria. Thus, a total of 7 publications were included in the review, with 5 studies comparing OS with AS with regard to MIO, pain, mandibular function movement, and postoperative clinical findings (clicking, TMJ tenderness, and crepitation) and 2 studies comparing ALL to simple AS with regard to MIO and pain.

AS was performed through an inferolateral approach (single-puncture technique). Using a trocar puncture, an outflow needle was placed through the skin 5 mm anterior to and slightly below the entry point of the trocar. The upper compartment of the TMJ was examined and irrigated with 100 mL lactated Ringer solution. Any fibrous adhesions were released in a semiblinded fashion, using a blunt trocar. A Moses elevator was then inserted into the superior joint compartment through the inferolateral portal to perform lateral eminence release and capsular stretch. Sodium hyaluronate was injected in the upper joint space at the end of the procedure in 2 studies and intracapsular betamethasone was injected in 1 study.

Concerning OS and operative arthroscopic procedures, several surgical procedures were performed: electrocautery of the pterygoid ligaments, myotomy of the lateral pterygoid muscle, motor debridement, and disk suturing in 2 studies; meniscoplasty, local repair of perforation, discectomy with or without disk replacement, arthroplasty, and high condylectomy or disk repositioning in the other studies.

Surgical procedures currently used for the treatment of internal derangement of the TMJ vary widely and include arthrocentesis and lavage, arthroscopy, arthrotomy, and even total TMJ replacement. According to the recommendations of the US National Institutes of Health, a noninvasive, conservative approach should be implemented for the patient with episodic signs and symptoms. For the patient with persistent, unremitting signs and symptoms, a stepwise approach is recommended. Surgical intervention is indicated only when nonsurgical therapy has been ineffective and when pain or dysfunction is moderate to severe. To the best of the author's knowledge, this is the first systematic review with meta-analysis comparing OS to AS and ALL to AS in the treatment of internal derangement of the TMJ.

Concerning OS versus AS, the results of the meta-analysis showed that OS provides superior pain reduction for patients compared with AS, and this is in agreement with previous studies. Although the results for MIO and mandibular function were also in favor of OS treatment, these results were not statistically significant. This is in accordance with the results of other studies.

Concerning AS versus ALL, there was a significant improvement in joint movement for patients managed with AS ($P<.001$). These results are consistent with those of other studies. This may be because, in addition to the function of lysis and lavage in the mediation of pain and inflammation, AS also releases the fibrous adhesion that interferes with functional jaw movements; this has been reported in other studies. However, there were no significant differences between the 2 groups with regard to pain reduction ($P=.53$), but the result favored the management of patients with ALL. This could be because lysis and lavage under high pressure is sufficient to remove inflammatory mediators and reduce pain.

This study has several limitations. Different OS approaches were performed and included in the OS group: discectomy, total or partial meniscoplasty with disk repair, high condylectomy with disk repositioning, and arthroplasty. In contrast, the same operative arthroscopic procedures were performed in the AS group. Thus, the variation in open-joint surgeries and different levels of joint pathology may have had an effect on the results of the present study. Hyaluronic acid injections were used in 2 studies, therefore there is a possible bias, as this may further enhance the effect of arthroscopic surgery.

Another potential weakness of this study is that only 3 were RCTs; 2 were CCTs; and 2 were retrospective studies. The 2 retrospective studies were included in the meta-analysis. Therefore, a sensitivity analysis was performed to assess the robustness of the results by repeating the analysis with the exclusion of the retrospective studies. After doing so, the overall results did not change. Most of the different open surgeries included in the OS group focused on the abnormal articular disk, and this was corrected surgically either by discectomy, total or partial meniscoplasty with disk repair, or by high condylectomy with disk repositioning. Therefore, the results of the present study emphasize the importance of disk position and shape in the treatment of internal derangement of the TMJ. This has been reported in other studies.

Not surprisingly, postoperative clinical findings such as clicking, joint tenderness/pain, and crepitation occurred less frequently following AS than OS; this is due to the incision and dissection or remodeling causing direct trauma to the fibrocartilage of the articular disk. Although, the results of the meta-analysis showed a trend toward better outcomes with OS for pain reduction and improvement of jaw function, AS is reported to be a minimally invasive surgery. Arthroscopy is a safe technique associated with only mild and transient complications, a more rapid patient recovery, and a short hospital stay. Other advantages of arthroscopic surgery are early mobilization of the jaw and no surgical dissection.

In the selection of the surgical procedure, another factor that may influence the therapeutic success is the preoperative duration of symptoms. A shorter preoperative duration of symptoms has been found to result in a more favorable therapeutic outcome in patients with OS. Early surgical intervention is more likely to result in

a successful therapeutic outcome for this procedure; therefore, the author suggests that TMJ surgery is indicated in patients who have failed to improve with ALL or AS.

In conclusion, the results of the meta-analysis showed OS was superior to AS in pain reduction in the management of internal derangement of the TMJ, with comparable MIO, jaw function, and clinical findings. In addition, the present study showed that ALL provides greater improvement in MIO and comparable pain reduction compared with AS.

A common open surgical procedure is disk replacement using autogenous free fat grafting. Shen et al[212] published a study evaluating the long-term survival rate of free fat in patients with patients who had undergone modified TMJ disk anchor, a common surgery in TMJ, to evaluate the signal intensity and volume changes using magnetic resonance imaging.

A total of 267 patients underwent TMJ open surgery over a half-year period (from January 2012 to June 2012) at the Ninth People's Hospital, Shanghai Jiao Tong University, School of Medicine; 133 patients (175 joints) were treated by modified TMJ disk anchor. Of these patients, 89 (117 joints) had more than 2 postoperative MRI examinations in the department, and 1 of the postoperative MRI examination was made just the day after operation. The following patients were excluded from this study; patients who underwent other kinds of TMJ surgeries; patients who had less than 2 postoperative MRI examinations; and patients who had MRI examinations in other departments. According to their latest follow-up MRI examination, the patients were divided into following groups: those 1 to 3 months (18 joints), 4 to 6 months (22 joints), 7 to 12 months (25 joints), 13 to 24 months (25 joints), and more than 24 months (27 joints) This study was conducted in accordance with the Ethics Committee of Shanghai JiaoTong University School of Medicine.

The formation of extensive fibrosis has been problematic after TMJ surgeries, such as total joint reconstruction, gap arthroplasty, discectomy, disk anchor, as well as other TMJ arthrotomies. Therefore it has drawn surgeons' attention to prevent adhesion after surgery. Many interpositional grafts have been reported since the 19th century, including autogenous and alloplastic materials. Among them, fat graft is one of the most common implants, which was first introduced in 1957 in the management of TMJ ankylosis. Since then, more and more attention has been paid to the use of fat grafts in this field. Fat graft has been used in such applications as TMJ ankylosis, discectomy, and disk anchor. Surgeons have considered that the use of autologous fat graft could minimize the occurrence of excessive fibrosis and provide an improved range of mandibular motion after total prosthetic TMJ reconstruction, and it has been reported that patients who underwent autogenous dermis-fat grafts following discectomy showed improvement in both mandibular mobility and function 1 year later. Abdominal dermis-fat grafts inhibit the growth of new bone and cartilage in the surgical management of TMJ ankyloses, and use of autogenous fat graft in TMJ provides excellent long-term clinical success.

Although many studies have revealed that autologous fat graft has achieved positive clinical effects in preventing fibrosis, the survival rate of grafted fat has still not been determined. In the present study, the authors calculated data for 117 joints to see the volume changes after surgery by MRI. The authors considered the volume the day after surgery as the total volume grafted, and the volumes at the other follow-up times were compared with that of the day after surgery. The results showed that the size was hovering right around 50%, although it reduced very slowly with long-term follow-up. In the 1 to 3 month group, the retention of grafted fat was 57.82% (50.59% to 68.77%), which supported the possibility that there might be an acute inflammatory period within 1 month, resulting in a sharp decrease in fat volume. Unfortunately, ethical considerations made it impossible to perform MRI within 1 month. Thus it was difficult to catch the volume changes in the early stages. However by more than 2 years' follow-up, it is considered that the grafted fat could survive, and the long-term survival rate was 48.44%.

The signal intensity of grafted fat was also evaluated in this study. Nearly half of the joints showed lower signal intensity of the grafted fat on MRI within 6 months. It is supposed that the viability of grafted fat was slightly depressed. However, compared with that of the day after surgery, the signal intensity recovered to normal 6 months later. The reacquired high signal intensity indicated that remodeling of the grafted fat might occur in the long term. The authors believe that free fat grafted into the TMJ cavity could live for a long time, based on the survival rate approximately 48.44%. However, the survival mechanism is still unknown and needs to be studied in the future.

Early treatment of TMJ problems can eliminate the need for the different joint surgeries described above. Lochbühler et al[213] discussed the arthritic involvement of the TMJ and the high prevalence in children which often results in joint damage and craniofacial growth disturbances. The unique anatomy of the mandibular condyle, with bone formation taking place from secondary cartilage directly beneath a thin fibrocartilage layer, makes the growth susceptible to effects related to other biological processes such as inflammation. Early detection and treatment of TMJ arthritis is considered essential to maintain normal development of the mandibular condyle and growth of the mandibular ramus in children. Local therapy with intra-articular corticosteroid injections is

effectively and safely used in peripheral joints and has also been introduced for TMJ arthritis. Although there is evidence for clinical and radiological improvement of TMJ arthritis following corticosteroid injections), there are no data, to the authors' knowledge, showing improvement or normalization of mandibular growth.

Because TMJ arthritis may frequently be asymptomatic and difficult to diagnose clinically, contrast-enhanced MRI is considered the gold standard for detecting early inflammatory involvement of the TMJ. In addition, MRI allows assessment of the level of inflammation, osseous deformity of the TMJ, and height of the mandibular ramus. The aim of this study was to assess whether intra-articular corticosteroid injections improve inflammation of the TMJ, prevent growth disturbances of the condyle, and restore normal growth of the mandibular ramus. This retrospective study included 33 consecutive children seen at a tertiary pediatric university hospital between June 2006 and November 2008, with a diagnosis of JIA according to the International League of Associations for Rheumatology 2003 criteria, MRI diagnosis of TMJ arthritis and subsequent corticosteroid injections during the same sedation. During this period, MRI of the TMJ was performed routinely at a time point when TMJ involvement had a potential implication for treatment.[16] Corticosteroid injections were performed regardless of symptoms or clinical findings when MRI indicated any degree of active inflammation represented by increased contrast enhancement of the TMJ.

The study population consisted of 23 girls and 10 boys, 2 to 9.7 years of age (5.3 ±1.9 years). All corticosteroid injections and MRI of the TMJ until early 2014 were evaluated. Follow-up MRI was usually performed at approximately 2 to 4 months after the corticosteroid injections and later at intervals around 6 to 12 months. When TMJ arthritis had not improved on follow-up MRI, corticosteroid injections were repeated. The corticosteroid injections) was performed by a pediatric rheumatologist without image guidance, but the location of the injected fluid into or around the TMJ was immediately evaluated by MRI. During the study period, the injected dose of triamcinolone hexacetonide varied from 6 mg to 20 mg per joint. All contrast-enhanced MRIs were performed at 1.5 Tesla. During the observation period, a total of 156 corticosteroid injections were performed. Two of the 66 TMJs were never injected, 19 TMJs were injected once, and 45 were injected repeatedly (2.4 ±1.4 corticosteroid injections per joint; range, 0 to 7 corticosteroid injections).

With this longitudinal study of 33 children with JIA and TMJ arthritis, immediate and long-term effects of local corticosteroid therapy by MRI over a median follow-up period of 5 years were demonstrated. To the author's knowledge, this is the first attempt to assess the outcome of corticosteroid injections to the TMJ by measuring mandibular ramus growth with MRI. In this study, repetitive corticosteroid injections could not improve the degree of osseous deformity of the TMJ. On the contrary, progressive deformity of the mandibular condyle and temporal bone in 41% of the investigated TMJ was observed.

Arvidsson et al[214] observed comparable progression of osseous deformities in 60 children (baseline mean 8.6 ±2.9 years of age) with JIA who had not been treated with repetitive corticosteroid injections, showing radiographic condylar and temporal bone abnormalities in 42% of patients (approximately 34% of TMJ) at baseline and in 65% of patients (approximately 60% of TMJ) at a 4-year follow-up examination. Compared with this older cohort (3 years on average), the grades of osseous deformity in this study tended to be lower at baseline but higher after a mean follow-up of 5 years. While this might be due to more severe inflammation in the selected patient group, it might also indicate that repetitive corticosteroid injections) accelerates the progression of osseous deformities of the TMJ. In this study, repetitive corticosteroid injections) was not able to restore normal growth of the mandibular ramus in the vast majority of inflamed TMJ, with the mean long-term growth rate over 5 years being significantly lower than normal.

The main limitations of the study are its retrospective nature, which did not allow for the control for the injected corticosteroid dose, and the lack of a control group of patients not treated with corticosteroid injections. However, comparison of TMJ with intra-articular and extra-articular location of the injected corticosteroid did allow demonstrating the effect of intra-articular corticosteroid on inflammatory activity and short-term growth. Further prospective studies comparing intra-articular injections with different doses of corticosteroids and placebo would be needed for better discriminating the effects of arthritis itself and corticosteroid on growth impairment of the mandibular ramus.

In children with JIA, repetitive corticosteroid injections to inflamed TMJ does not prevent progressive osseous deformity of the mandibular condyle and cannot restore normal growth of the mandibular ramus. Repetitive intra-articular application of corticosteroid may result in even more pronounced destruction and growth reduction of the mandibular condyle than that caused by arthritis alone. Because the goal of treatment was not reached in these patients, the authors have discontinued the use of corticosteroid injections) on the TMJ treated at their institution.

Lavi et al[215] authored a paper discussing tissue engineering related to the TM disk. Tissue engineering and regenerative medicine may constitute a promising therapeutic approach, with resident stromal progenitor cells a key factor in the process.[216] The author hypothesized that the TMJ disk contains multipotent stromal progenitors

that may play an important lesson to role in regeneration of the disk. TMJ disk cells were cultured and evaluated for growth kinetics and colony-forming units (CFUs). Single cell-derived clones were isolated and induced to differentiate toward the osteogenic, adipogenic and chondrogenic lineages by culturing in various induction media. Flow cytometry was used to identify multipotent stromal cell surface markers in additional cell specimens, and reverse transcription polymerase chain reaction was used to determine gene expression patterns within isolated cells. High numbers of CFUs were observed, indicating cell self-renewal. Biochemical assays showed significantly higher alkaline phosphatase (ALP) activity, lipid droplet concentration, and glycosaminoglycan levels in cells cultured in osteogenic, adipogenic, and chondrogenic induction medium, respectively. Approximately 1% of the total cell population demonstrated the capability to differentiate into all 3 mesenchymal lineages. Chondrogenic gene levels within TMJ disk-derived cells were significantly reduced in passaged culture. These results support the hypothesis that multipotent stromal progenitor cells populate the TMJ disk and possess proliferation and differentiation capabilities. These cells may contribute to the regeneration potential of dysfunctional tissue and become the primary component in future attempts at tissue engineering or regeneration of the TM disk.

SLEEP-DISORDERED BREATHING

Oral appliance therapy is moving toward mainstream for the treatment of obstructive sleep apnea. The interrelationship with medicine is growing as well. Sleep dentistry is increasingly part of sleep medicine educational offerings. The literature reviewed clearly shows the value oral appliance therapy can bring to a patient's life. Medicine requires a higher level of proof than is common in dentistry. The dentist must be aware that medicine does not recognize conjecture and hypothesis. Outcome studies drive opinion, and we in dentistry must strive to assure the treatments rendered are coincident with what has been published. It is clear that the effectiveness of oral appliance therapy can change with time. It is the dentist's responsibility to carefully monitor the patient long-term with testing and medical consultation. The days of placing an oral appliance for "snoring" without appropriate testing are long past.

Oral appliance therapy

One study[216] explored the effect of a mandibular advancement device on tongue shape in patients with obstructive sleep apnea, and how the shape changes impacted responses to treatment. A cohort of 68 adults with symptomatic mild to severe obstructive sleep apnea were followed. They received custom-fabricated mandibular advancement devices and treatment results were determined by polysomnography (PSG). Sagittal and axial 2-dimensional MRIs were acquired with and without the appliance in situ. Data collected included tongue height, length, width, area, and shape (defined as height/length). Measurements of surrounding upper airway structures were also recorded, including soft palate length, width and area; airway area, length and minimum width. Forty-seven of the 68 patients were designated responders to therapy, with a $\geq$50% reduction in apnea-hypopnea index; 21 were nonresponders with less than a 50% drop in apnea-hypopnea index. With the mandibular advancement device in place, there was no change in sagittal tongue area; however, most of the values of tongue shape did demonstrate change. The responders exhibited a greater decrease in tongue length with the appliance than the nonresponders. The authors concluded that mandibular advancement device therapy does induce changes in tongue shape. Further study is warranted to elucidate the effect of tongue position on a patient's response to treatment.

Another group[217] evaluated horizontal protrusion and vertical opening on upper airway measurements in dentate participants with apnea. They used 5 different mandibular advancement device designs in 9 adult patients with obstructive sleep apnea, and MRI was performed to determine the area of the entire pharynx (velopharynx, oropharynx, hypopharynx); dimensional changes were noted and compared. The mandibular advancement devices that were set at 75% of maximum mandibular protrusion with 5 mm of vertical opening and 75% of maximum mandibular protrusion with 10 mm of vertical opening were shown to induce statistically significant dimensional change within the upper airway compared with the other 3 devices. Within the limitations of their small sample size, the authors concluded that the amount of mandibular protrusion impacts the dimensions of the pharynx while the vertical dimension contributes no significant changes in the sagittal dimension.

A different trial[218] sought to use drug-induced sedation endoscopy (DISE) to explore sites and mechanisms of residual airway collapse following an incomplete response to mandibular advancement device therapy. Thirty-five consecutively screened obstructive sleep apnea patients with continuous positive airway pressure (CPAP) therapy intolerance and incomplete response to oral appliance therapy were evaluated. They underwent DISE with and without the oral appliance in place. At baseline, all individuals exhibited airway collapse at multiple levels. The soft palate was the most common site of oral appliance therapy failure, with 42.9% (15) exhibiting velum collapse; 20% of the patients (7) had persistent collapse of the epiglottis. Twenty-three participants were offered surgery to augment oral appliance therapy; 20 underwent additional therapy including

appliance adjustment or cervical positional therapy. Mean apnea-hypopnea index was reduced from 37.4 at baseline, to 16.4 with oral appliance therapy and to 10.7 following intervention based on DISE results. It was concluded that DISE with and without an appliance in place may guide the patient to other treatment options to augment the treatment result with oral appliance therapy.

A retrospective study[219] was conducted to evaluate medium long-term treatment outcomes of oral appliance therapy for patients with severe obstructive sleep apnea. Fifty-two participants with an apnea-hypopnea index ≥40 who were CPAP-intolerant received a custom-fitted modified oral appliance (Herbst). A 2-year average follow-up including PSG was performed in 36 of the individuals. Baseline apnea-hypopnea index for the group was 55.25 ±10.79; at the follow-up PSG, apnea-hypopnea index was 17.74 ±11.0 for the 36 patients who underwent the second sleep study. Fifty-three percent (n=19) reached an apnea-hypopnea index <15. This study concluded that oral appliances were successful at treating severe obstructive sleep apnea in those for whom initial CPAP therapy failed.

Another group set out to determine claustrophobia frequency in adults with obstructive sleep apnea after first CPAP night, and examine whether claustrophobia impacts CPAP non-adherence.[220] Secondary analysis of prospective, longitudinal study of 97 adults with obstructive sleep apnea were performed. CPAP-Adapted Fear and Avoidance Scale (CPAP-FAAS) surveys which evaluate claustrophobic tendencies were collected immediately after the CPAP titration PSG. The primary outcome measured was CPAP use at 1 week and 1 month. Sixty-three percent of users had claustrophobic tendencies, with women having higher CPAP-FAAS than men. FAAS scores ≥25 are indicative of claustrophobic tendencies and impacts CPAP nonadherence at 1 week and less CPAP use at 1 month when adjusting for mask style and BMI. Claustrophobia is prevalent in CPAP users and influences short-term and longer-term nonadherence.

Taiwanese researchers[221] explored the effects of mandibular advancement device therapy on serum levels of nitric oxide (NO) derivatives and endothelial function by endothelium-dependent flow-mediated dilation (FMD) in obstructive sleep apnea syndrome. Thirty patients with moderate to severe obstructive sleep apnea syndrome treated with mandibular advancement device therapy and 15 healthy control participants were prospectively enrolled. All individuals completed PSG, which was repeated 2 months after mandibular advancement device treatment in the obstructive sleep apnea syndrome group. FMD was measured by high-resolution B-mode ultrasonography, and serum NO levels were tested using enzyme-linked immunosorbent assay to analyze the blood samples. At baseline, serum NO level and FMD were lower in patients with obstructive sleep apnea syndrome than that in controls. Following 2 months of mandibular advancement device therapy, the responders demonstrated an increase in serum NO levels from 11.8 ±5.8 μM pretreatment to 22.7 ±4.9 μM post mandibular advancement device. The flow-mediated dilation increased from 5.0 ±4.6 pre-treatment to 10.5 ±4.8 post-mandibular advancement device. The nonresponders showed no change in the NO and FMD parameters. The authors concluded that endothelial function can be improved following effective appliance therapy treatment for patients with obstructive sleep apnea syndrome.

A different study sought to examine the effect of oral appliance therapy on blood pressure in a group with obstructive sleep apnea and prehypertension.[222] Thirty-seven patients were followed; they underwent PSG pretreatment, and at 3 months and 1 year. Blood pressure was recorded at the same appointments. At 3 months follow-up, they found an average decrease of 9.35% in systolic blood pressure (SBP) and 11.04% in diastolic BP (DBP); snoring index decreased by 80.31% and apnea-hypopnea index by 83.93%, whereas the sleep apnea quality of life (SAQOL) scores improved by a dramatic 183.9%. At 1 year, the SBP was 12.16% lower, and the DBP was 14.01% lower; the snoring index dropped by 82.52% and the apnea-hypopnea index decreased by 89.77%. SAQOL was 240% better at 1 year. The results of this study need to be interpreted with caution because of the dramatic treatment results reported; repeatable results from different studies will help to bolster this study.

A 10-year follow-up prospective study set out to evaluate the effects of treatment with a mandibular advancement device in patients with obstructive sleep apnea or snoring.[223] Seventy-seven consecutive patients with obstructive sleep apnea or snoring were treated with oral appliance therapy. At baseline and 10-year follow-up, sleep quality questionnaires and polygraphic examinations were administered; weight and neck size were also measured. The authors evaluated 64 of the 77 patients at the 10-year mark; 45 participants were using mandibular advancement device, 9 were using CPAP, and 10 had no treatment. For the oral appliance group, 89% reported using the device nightly, and 9% several nights a week. Compared with baseline, the oral appliance group had a substantially lower oxygen desaturation index and increased lowest arterial oxygen saturation (SaO_2, nadir) after 10 years. Mandibular advancement device treatment was deemed successful for 70% of the patients, even though 89% subjectively considered themselves cured, so treatment effect overestimation needs to be considered. Those who responded to mandibular advancement device therapy maintained baseline weight and neck size, while nonresponders

showed increases in both parameters. The researchers concluded that long-term oral appliance therapy is well tolerated and effective, and weight gain may compromise treatment outcomes.

A systematic literature review was performed[224] to explore the predictive value of cephalometric examination for oral appliance therapy treatment outcomes in adult obstructive sleep apnea patients. The authors searched MEDLINE, Google Scholar, Scopus, and Cochrane Library databases through December 2014, as well as the references from pertinent articles. Two review authors independently evaluated eligibility, extracted data, and determined quality of the studies. Fifteen studies met the inclusion criteria; they found that most of the skeletal, dental, and soft tissue cephalometric measurements were widely recognized as not prognostic for mandibular advancement device treatment response. They concluded that currently available evidence is insufficient for identification of cephalometric parameters capable of reliably selecting between poor and good responders to oral appliance therapy for obstructive sleep apnea. They noted methodological weaknesses of these studies to determine possible future areas of research.

Another group[225] sought to verify the usefulness of complete dentures modified as a mandibular advancement device in positively influencing pharyngeal volume to treat obstructive sleep apnea in patients with edentulism. Seventeen individuals were evaluated (12 men, 5 women; average 61 ±4 years of age; BMI=22 ±5; apnea-hypopnea index=15 to 30). All patients had worn the prostheses for at least 1 year, and all had them modified into a mandibular advancement device. They were evaluated preoperatively and again 6 months after using the appliance, measuring sleep efficiency, apnea-hypopnea index, oxygen desaturation events per hour, mean oxygen saturation, snoring index, and airway volume. They found that the airway volume without any prosthesis or appliance in place was reduced as compared with having the unaltered prostheses in place; the modified denture mandibular advancement device conferred the largest airway dimension. Increased volume was most pronounced in the velopharyngeal region, and obstructive sleep apnea symptoms were reduced. The authors acknowledge the small sample size, so the conclusions are inferred, and larger sample sizes will help to validate the findings.

One clinician[226] set out to evaluate the long-term efficacy of oral appliances in patients treated early with obstructive sleep apnea. Eight men and 1 women with a median 68.1 years of age and a median treatment time of 16.5 years were included. They were assessed with PSG without and with an oral appliance in place at the outset of treatment and again after a minimum of 15 years of continuous treatment. The apnea-hypopnea index decreased from a median of 17.3 to 7.2 at the short-term follow-up; after long-term use, the apnea-hypopnea index was 32.4 without the appliance and 35.1 with the appliance. The degree of mandibular advancement did not differ between the 2 study evaluations. The author emphasizes regularly scheduled follow-up with updated sleep apnea recordings to confirm continued treatment success and avoid suboptimal outcomes or treatment failure over time.

A narrative review examines efficacy versus effectiveness in relation to CPAP and oral appliance treatment of obstructive sleep apnea.[227] Efficacy is defined as how well an intervention works under ideal conditions, whereas effectiveness is how well an intervention performs in the real world where conditions are not controlled. CPAP is standard first-line treatment for obstructive sleep apnea; it is highly efficacious but has many limitations, including suboptimal patient acceptance and adherence rates, which degrade the desired health benefits. Patients often report preferring oral appliances over CPAP therapy, with higher compliance rates. However, interindividual variability in the efficacy of oral appliance therapy means that patients are often left with some residual obstructive sleep apnea. Similar results in terms of health outcomes (sleepiness, quality of life, driving performance, and blood pressure) suggest that although the 2 treatments have different efficacy and treatment usage profiles, they result in similar overall effectiveness.

A systematic review and meta-analysis examined CPAP versus mandibular advancement device and effect on blood pressure in patients with obstructive sleep apnea.[228] The authors compared the association of CPAP, mandibular advancement devices and inactive control groups (placebo or no treatment) with changes in SBPand DBP n patients with obstructive sleep apnea. They searched MEDLINE, EMBASE, and the Cochrane Library databases through the end of August 2015 to review study bibliographies. Of 872 initial possibilities, they selected 51 randomized clinical trials for analysis. Of the 51 studies analyzed (total sample size of 4888 patients), 44 compared CPAP with an inactive control; 3 compared mandibular advancement devices with an inactive control; 1 compared mandibular advancement device with continuous positive airway pressure; and 3 compared CPAP, mandibular advancement devices and an inactive control. Compared with an inactive control, CPAP was associated with a drop in SBP of 2.5 mm Hg and in DBP of 2.0 mm Hg. A 1-hour-per-night increase in mean CPAP use was associated with additional benefit on blood pressure. Compared with an inactive control, mandibular advancement devices were associated with a reduction in SBP of 2.1 mm Hg and in DBP of 1.9 mm Hg. No statistically significant difference was found between mandibular advancement devices and CPAP in their association with dropping SBP and DBP.

Another randomized, 2-period crossover trial compared the effects of mandibular advancement device therapy with CPAP on daytime cardiac autonomic function in a wide range of individuals with obstructive sleep apnea.[229] Forty patients underwent treatment with mandibular advancement device and with CPAP for 12 weeks each. The participants underwent PSG at baseline and after each treatment increment as well as a daytime cardiac autonomic function test that measured heart rate variability, continuous blood pressure, and baroreceptor sensitivity under conditions of spontaneous breathing, with breathing at 6, 12, and 15 per minute. Both of the therapies were found to substantially eliminate apneas and hypopneas, with CPAP having a greater effect. During daytime, with all 4 conditions of controlled breathing, 3-minute mean values of continuous DBP were significantly reduced for both mandibular advancement device and PAP therapy. Selective increases due to therapy with mandibular advancement device were found for heart rate variability high frequency (that is, parasympathetic activity) values. No changes were documented for baroreceptor sensitivity in either mode of treatment. The authors concluded that both the mandibular advancement device and CPAP result in similar beneficial changes in cardiac autonomic function during the daytime.

A Swiss group[230] performed a network meta-analysis comparing the effects of CPAP and mandibular advancement devices on sleepiness in patients with obstructive sleep apnea. Excessive daytime sleepiness is the most important symptom of obstructive sleep apnea syndrome and impacts work productivity, quality of life, and risk for automobile accidents. They set out to quantify the effects of the 2 main treatments for obstructive sleep apnea on excessive daytime sleepiness. They explored MEDLINE and the Cochrane Library through May 31, 2015, to identify RCTs comparing the effects of CPAP, mandibular advancement devices or an inactive control (placebo or no treatment) on the Epworth Sleepiness Scale (Epworth sleepiness scale; range 0 to 24 points) in individuals with obstructive sleep apnea. Sixty-seven studies with 6873 participants were used in the meta-analysis. Compared with an inactive control, CPAP was associated with a reduction in Epworth sleepiness scale score of 2.5 points and mandibular advancement devices a reduction of 1.7 points. It is noteworthy that studies that reported higher CPAP adherence also reported larger treatment effects. They concluded that both of these therapies are effective methods for reducing excessive daytime sleepiness in patients with obstructive sleep apnea; CPAP may confer a greater benefit on those with more severe obstructive sleep apnea or daytime sleepiness than on controls.

A different meta-analysis of RCTs of mandibular advancement devices and CPAP for obstructive sleep apnea was done to explore the treatment effectiveness relative to disease severity.[231] MEDLINE, Embase, and Scientific Citation Index were searched through August 2013; 77 RCTs were identified that compared mandibular advancement device with conservative management; mandibular advancement device with CPAP, or CPAP with conservative management. Overall, mandibular advancement devices and CPAP substantially improved apnea-hypopnea index; in direct comparisons, mean apnea-hypopnea index and Epworth sleepiness scale were lower for CPAP. In comparison with conservative management, both mandibular advancement device and CPAP reduced Epworth sleepiness scale similarly, even though there were no CPAP versus mandibular advancement device trials in mild obstructive sleep apnea. The authors concluded that both therapies are clinically effective in the treatment of obstructive sleep apnea-hypopnea; CPAP has a greater treatment effect, but mandibular advancement device is an appropriate modality for patients who are CPAP intolerant.

A systematic review evaluated the effectiveness of mandibular advancement appliances in treating obstructive sleep apnea.[232] MEDLINE, Scopus, and Cochrane Library databases were searched, resulting in 22 articles published since 2005 that met their quality and inclusion criteria. Using mandibular advancement devices during sleep helps to prevent snoring and excessive daytime sleepiness, reduces the apnea-hypopnea index significantly, and brings about beneficial alterations in the upper airway. Adjustable and custom-made appliances deliver better results than prefabricated devices; Monobloc appliances give rise to more adverse events, which are typically found to be mild and transient. The authors conclude that mandibular advancement devices increase the upper airway area by bringing the soft palate, tongue and hyoid bone forward and activating the masseter and submental muscles, thereby preventing closure. These effects collectively reduce the apnea-hypopnea index, increase oxygen saturation, and improve the main symptoms of obstructive sleep apnea/hypopnea syndrome (OSAHS).

Another group provides an overview and quality assessment of systematic reviews concerning mandibular advancement splint therapy for obstructive sleep apnea.[233] The investigators searched PubMed and relevant Cochrane Library databases to select systematic reviews investigating the response of adults with OSAHS to mandibular advancement splint treatment. The quality of the reviews was assessed using AMSTAR, a validated tool for assessing quality. Eight systematic reviews were identified exploring both subjective and objective outcome measures. The effectiveness of mandibular advancement device therapy was compared with no treatment (n=1), nonactive appliance (N=6), CPAP (n=5), surgical intervention (n=3), and an alternative mandibular advancement splint treatment (n=4). The quality of

the reviews varied from 3 to 11 with a median of 7, with only 2 of higher quality (with an AMSTAR score >10). One of the Cochrane reviews was deemed high quality and found substantial benefits of mandibular advancement splint therapy as compared with inactive appliances in terms of excessive daytime sleepiness and objective apnea-hypopnea index outcomes. They recommend that current reporting guidelines for systematic reviews (for example PRISMA) and sources of high-quality existing reviews should be closely monitored to enhance the validity and relevance of future reviews.

A different systematic review examined current evidence regarding the CV benefits of oral appliance therapy for obstructive sleep apnea patients.[234] PubMed, Web of Science, MEDLINE, and OvidSP databases were searched for relevant articles prior to January 20, 2013 that examined the effects of oral appliance therapy on any cardiovascular parameters (including BP, endothelial function (EF), and left ventricular (LV) function of the heart). Eleven articles were included in the systematic review. Seven of 8 studies showed a significant reduction in BP with a mean BP decrease of 4.2 mm HG; 2 studies demonstrated significant improvement in EF; 1 study exhibited substantial improvements in LV heart function. They concluded that oral appliance therapy showed beneficial effects on cardiovascular comorbidity in participants with obstructive sleep apnea. In studies comparing oral appliances with CPAP therapy, the effects of oral appliance therapy were in the same order of magnitude as the effect of CPAP treatment.

A Spanish group[235] produced a case report concerning the development of pneumoparotid associated with an mandibular advancement device for obstructive sleep apnea. A 42-year-old man with moderate obstructive sleep apnea who was CPAP-intolerant was treated with a mandibular advancement device. After 3 months of therapy, he complained about right subauricular swelling with moderate pain and tenderness. Clinical examination revealed that he was afebrile, with right submandibular angle swelling, pain, and subcutaneous crepitus. Ultrasound and noncontrast facial CT scan showed the presence of air bubbles in the right parotid and gas along the right Stenson duct. The only cause of pneumoparotid in this patient was the blowing and whistles at night related to the appliance. This device may induce resistance to expiration, contributing to an increase in intraoral pressure. They reported that this side effect of mandibular advancement device therapy had not been previously described.

Another clinical report discusses the treatment of severe obstructive sleep apnea with a combination therapy of oral appliance therapy and hypoglossal nerve stimulation (HNS).[236] The authors highlight a patient who had incomplete treatment success with an oral appliance. Following the surgical implantation of a hypoglossal nerve stimulation device, they reintroduced oral appliance therapy. Symptoms and objective control of breathing were normalized compared with partial resolution with either modality. Titration of each device was minimized because of the combination therapy. They claim that this is the first reported patient with a combination oral appliance therapy and HNS. An oral appliance design with adequate anterior space to accommodate tongue protrusion during active stimulation should be considered in HNS patients.

Pathophysiology and medical implications

One study[237] sought to investigate the association between upper airway (upper airway) abnormalities and inspiratory flow limitation (IFL) in patients with mild sleep-related breathing disorder (SRBD). IFL is defined as a "flattened shape" of inspiratory airflow contour detected by nasal cannula pressure during sleep and can be a hallmark of elevated upper airway resistance, especially in mild SRBD. A total of 754 participants were divided into 4 groups: (1) apnea-hypopnea index <5 (no sleep apnea) and <30% of total sleep time (TST) with IFL (515 individuals); (2) apnea-hypopnea index <5 and >30% of TST with IFL (46 people); (3) apnea-hypopnea index 5-15 and <30% of TST with IFL (168 participants); and (4) apnea-hypopnea index 5-15 and >30% of TST with IFL (25 individuals). Those with complaints of oral breathing exhibited a risk 2.7-fold larger of being group 4 compared with group 3. Nasal structural abnormalities increased the chances of being in group four 3.2-fold in comparison with group 1. Individuals with voluminous lateral wall demonstrated a risk 4.2-fold larger of being group 4 compared with group 3. The authors concluded that patients with >30% of TST with IFL detected in sleep studies may have had nasal and palatal anatomic abnormalities in mild SRBD.

An MRI study using diffusion-weighted pseudo-continuous arterial spin labeling (DW-pCASL) was undertaken to examine water exchange across the blood-brain barrier (BBB) in obstructive sleep apnea.[238] Individuals with obstructive sleep apnea show brain injury in sites that control autonomic, cognitive, and mood functions. The processes leading to injury may include altered BBB actions. DW-pCASL imaging was performed in 9 patients with obstructive sleep apnea and 9 controls. Global mean gray and white matter arterial transit time, water exchange rate across the BBB, DW-pCASL ratio, and cerebral blood flow values were compared between the 2 groups. They found that obstructive sleep apnea patients show compromised BBB function, but intact large artery integrity. The BBB changes may contribute to neural damage leading to abnormal function in obstructive sleep apnea and suggest a need to repair BBB function with strategies commonly used in other areas of medicine.

Another imaging study[239] explored the effect of cerebrovascular stressors such as breath holding or CO_2 on global magnetic resonance imaging signal changes. Nine participants performed the Valsalva maneuver (a standard clinical tool that consists of an exhalation against a closed glottis or another closed system, with the goal of increasing intrathoracic pressure to 20 to 40 mm Hg) during function MRI (fMRI) data collection. Expiratory pressures ranged from 10 to 40 mm Hg. Breath holds ending on either inhalation or exhalation were also gathered. The maximal and minimal fMRI signal scaled with thoracic pressure load, and the overall amplitude of responses to the maneuver varied, depending on brain tissue. Moreover, a Valsalva effort as short as 5 seconds yielded signal changes similar in spatial distribution and magnitude to a 20-second breath hold. The authors note that the Valsalva maneuver may have applications for calibrated fMRI trials.

A different study[240] set out to evaluate the influence of different stimulus durations on arousal frequency during different sleep stages, based on the knowledge that a pure nasal trigeminal stimulus leads to arousal during sleep. Ten young healthy volunteers underwent 20 nights of polysomnography each for the study. Pure trigeminal stimulation with both different concentrations of CO_2 (0, 10, 20, 40%v/v) and different stimulus durations (1, 3, 5, 10 seconds) were applied during different sleep stages to the participants using an olfactometer. The applications were performed during light sleep, deep sleep, and REM sleep. They demonstrated that the number of arousals increased with rising stimulus duration and stimulation concentration during each sleep stage, confirming that trigeminal stimuli during sleep led to arousals in a time- and dose-dependent fashion.

Another group[241] sought to determine the diagnostic accuracy of predicting obstructive sleep apnea based on anatomic and nonanatomic traits; they also tried to predict the number of patients with obstructive sleep apnea who might be effectively treated without CPAP based on these traits. Fifty-seven individuals with and without obstructive sleep apnea underwent standard clinical and research sleep studies to assess obstructive sleep apnea severity and the physiological traits important for obstructive sleep apnea pathogenesis, respectively. The traits were incorporated into a physiological model to predict obstructive sleep apnea. The model was validated by comparing the model prediction of sleep apnea with the clinical diagnosis of sleep apnea. A simulation was then performed to evaluate various trait manipulations to predict the number of patients treated by each intervention. The model was found to have good sensitivity (80%) and specificity (100%) for predicting obstructive sleep apnea. A single intervention on 1 trait would be predicted to treat sleep apnea in approximately one quarter of all patients. Combination therapy with 2 interventions was predicted to treat obstructive sleep apnea in 50% of the patients. The authors conclude that nonanatomic traits are important factors in obstructive sleep apnea pathogenesis and the effectiveness of non-PAP therapies.

Investigators explored physiologic determinants of the respiratory arousal threshold to develop a clinical tool that can identify patients with low arousal threshold.[242] A low respiratory arousal threshold is implicated in obstructive sleep apnea pathogenesis and may be a therapeutic target. A total of 146 participants underwent overnight polysomnography with an epiglottic catheter to measure the arousal threshold (nadir epiglottic pressure before arousal). The threshold was evaluated from up to 20 non-rapid eye movement (NREM) and rapid eye movement (REM) respiratory events selected randomly. Statistical analysis was performed to determine the independent predictors of the arousal threshold and develop a clinical scoring system. Lowest oxygen saturation as measured by pulse oximetry, apnea-hypopnea index, and the fraction of events that were hypopneas were independent predictors of the arousal threshold. Using logistic regression on these variables, they were able to correctly predict a low arousal threshold in 84.1% of individuals, with a sensitivity of 80.4% and a specificity of 88.0%. This finding could facilitate larger interventional studies targeting the arousal threshold.

The same research group used polysomnography alone to create a novel method of estimating loop gain in patients with obstructive sleep apnea.[243] Hyperresponsive ventilatory control leads to elevated loop gain, which is a primary nonanatomic cause of obstructive sleep apnea; spontaneous ventilatory fluctuations due to apneas and hypopneas lead to opposing changes in ventilatory drive as determined by loop gain. Fitting a simple ventilatory control model including chemical and arousal inputs to the respiratory drive to the ventilatory pattern can reveal the underlying loop gain. They tested their method in individuals with obstructive sleep apnea by comparing with a standard method (CPAP drop method) and by assessing its ability to detect the known reduction in loop gain with oxygen and acetazolamide. Twenty-eight participants had baseline PSG-correlated versus CPAP-estimated loop gain; detected the known drop in loop gain with oxygen in 11 participants and with acetazolamide in 11 participants; and predicted the obstructive sleep apnea response to loop gain-lowering therapy. They concluded that their method could identify like responders to therapies targeting ventilatory control.

A review article[244] examined the role of high loop gain induced by intermittent hypoxia in the pathologic course of obstructive sleep apnea. intermittent hypoxia and unstable breathing are key features of obstructive sleep apnea. Unstable ventilatory control can be due to high loop gain and likely leads to cyclical airway

obstruction by promoting airway collapse during times of low-ventilatory drive. Potential therapeutic strategies to treat obstructive sleep apnea include interventions designed to lower loop gain; however, the contribution of inherent versus induced loop gain abnormalities in sleep apnea remains uncertain. Therefore, a better insight into the mechanisms causing elevated loop gain in obstructive sleep apnea is needed to guide the design of loop gain-based therapies. Individuals with obstructive sleep apnea demonstrate abnormal chemoreflex control which contributes to elevated loop gain. These abnormalities have been shown to normalize after CPAP therapy, hinting at induced rather than inherent trait abnormalities.

Experimental intermittent hypoxia, simulating obstructive sleep apnea, increases hypoxic chemosensitivity and induces long-term facilitation, a prolonged increase in ventilatory neural output which outlasts the original stimulus. These neuroplastic changes induce the same abnormalities in chemoreflex control as seen in patients with sleep apnea. This review outlines the evidence to support that a critical component of high loop gain in obstructive sleep apnea is triggered by intermittent hypoxia and is reversed by preventing the intermittent hypoxia.

A systematic review and meta-analysis[145] evaluates the association between sleep-disordered breathing/obstructive sleep apnea and cancer incidence. The investigators searched MEDLINE, Embase, Cochrane Central, and electronic databases for relevant studies in any language. Inclusion criteria consisted of: those on patients with sleep-disordered breathing/obstructive sleep apnea; those reporting cancer incidence rates specific to patients with sleep-disordered breathing/obstructive sleep apnea; and those defining sleep-disordered breathing/obstructive sleep apnea using polysomnographic measures. The quality of the selected studies was assessed using the Newcastle-Ottawa Quality Assessment Scale (NOQA). Of 8766 possible citations, 5 studies that defined sleep-disordered breathing/obstructive sleep apnea using the apnea-hypopnea index or the respiratory disturbance index totaling 34 848 patients with sleep disordered-breathing and 77 380 patients without sleep-disordered breathing were pooled into a meta-analysis. All 5 studies were of good quality, with an NOQA score of $\geq$6. A total of 574 (1.6%) and 290 (0.37%) incident cancers were reported in patients with and without sleep-disordered breathing, respectively. In the unadjusted analysis, airway patients were at an increased risk of incident cancer (relative risk: 1.53) when adjusting for conventional cancer risk factors and the association between sleep-disordered breathing/obstructive sleep apnea and cancer incidence, although attenuated (relative risk: 1.40) remains significant. The authors concluded that sleep-disordered breathing may increase the risk of incident cancer; they caution that inferring an independent association is not possible from the analysis performed considering the retrospective cohort design of the included studies and high interstudy heterogeneity.

A different review[245] also investigated the association between obstructive sleep apnea and the development and progression of cancer. The authors note that recent epidemiological surveys suggest that patients with obstructive sleep apnea have a higher incidence of cancer and cancer-related mortality than patients without sleep apnea. Animal studies have shown that the activation of the HIF-I and VEGF pathways in response to intermittent hypoxia may promote the blood supply which contributes to tumor growth. Moreover, tumor-associated macrophages may be changed by intermittent hypoxia (or sleep fragmentation) to a tumor-promoting phenotype leading to more aggressive cancer behavior. They conclude that the relationship between obstructive sleep apnea and cancer has been confirmed, with sleep apnea patients having a relative high prevalence of cancer and cancer-related mortality. obstructive sleep apnea promoting cancer development and progression may be related to intermittent hypoxia and sleep fragmentation. They note that more clinical data and basic studies are warranted to explain and confirm the relationship between cancer and obstructive sleep apnea.

Another study[246] set out to explore the prevalence and relationship of microalbuminuria with clinical and physiological parameters in patients with obstructive sleep apnea syndrome. Microalbuminuria is known as a risk factor for CVD, and may be present as a result of intermittent hypoxemia in patients with obstructive sleep apnea. Ninety-eight individuals with obstructive sleep apnea syndrome and 26 nonapneic snoring participants diagnosed through PSG were included. The urinary albumin-to-creatinine ratio (UACR) was calculated according to a previously described formula. The modified cumulative illness rating scale (MCIRS) was used to evaluate the severity index of chronic diseases. Insulin resistance method was analyzed by homeostasis assessment model for insulin resistance (HOMA-IR). Subjective sleepiness was measured using the Epworth sleepiness scale. Body mass index, MCIRS, and UACR were higher in participants with obstructive sleep apnea syndrome than nonapneic snoring participants. In the linear regression model, a negative relationship between UACR and minimal O_2, and a substantial positive relationship between UACR and desaturation index. They concluded that microalbuminuria could be seen in patients with obstructive sleep apnea syndrome based on the severity of disease and hypoxemia; these patients should be regularly followed for risk of CV morbidity or mortality.

A different group[247] investigated the prospective relationship of asthma with incident obstructive sleep apnea. They analyzed data gathered from the Wisconsin Sleep Cohort Study (a population-based prospective epidemiologic study beginning in 1988). Adult participants were recruited from a random sample of Wisconsin state employees to attend overnight PSG studies at 4-year intervals; asthma and covariate information were evaluated during PSG studies through March 2013. Eligible participants were identified as free of obstructive sleep apnea, with an apnea-hypopnea index <5 and not treated, by 2 baseline PSG studies. There were 1105 4-year follow-up intervals provided by 547 participants (52% female; mean ±SD baseline age, 50 ±8 years). Repeated-measures Poisson regression with adjustment for confounders was undertaken to assess the associations of presence and duration of asthma with 4-year incidences of both obstructive sleep apnea and obstructive sleep apnea with accompanying chronic daytime sleepiness. Twenty-two of 81 participants (27%) with asthma developed incident obstructive sleep apnea over their first observed 4-year follow-up interval compared with 75 of 466 participants (16%) without asthma. Using all 4-year intervals, participants with asthma experienced 45 cases of incident obstructive sleep apnea during 167 four year intervals (27%) and those without asthma experienced 160 cases of incident obstructive sleep apnea during 938 4-year intervals (17%). Controlling for sex, age, baseline, and change in BMI, the corresponding adjusted relative risk was 1.39. Asthma was associated with an increased risk of new-onset sleep apnea, as well as obstructive sleep apnea syndrome. They call for further studies to explore the mechanisms underlying this association, as well as regular examinations for obstructive sleep apnea development in patients with asthma.

A clinical review[248] examined the connections between CV autonomic dysfunctions and sleep disorders. Animal and human research has demonstrated that disorders of the autonomic nervous system may impact sleep physiology; conversely, sleep disorders may be associated with autonomic dysfunctions. This review discussed the clinical presentation, supposed pathogenetic mechanisms, and the diagnostic and prognostic impact of altered cardiovascular autonomic control in sleep disorders. This dysfunction may be due to a common pathogenetic mechanism affecting both autonomic cardiovascular control and sleep, as in fatal familial insomnia, or it may be primarily attributed to the sleep disorder, as in obstructive sleep apnea. The authors claim that the available data suggest that a systematic assessment of the relationship between sleep disorders and impaired autonomic control of the cardiovascular system is warranted.

Another study from the Wisconsin Sleep Cohort Study[249] attempted to determine the association of objectively measured sleep-disordered breathing with coronary heart disease (CHD) or heart failure (HF) in a nonclinical population. A longitudinal analysis of a community-dwelling cohort was followed for up to 24 years. The cohort consisted 1131 participants who completed 1 or more overnight PSG studies; they were free of CHD or HF at baseline, were not treated by CPAP, and were followed over 24 years. In-laboratory PSG assessed sleep-disordered breathing status, based on the number of apnea and hypopnea events per hour of sleep; incident CHF or HF was defined by new reports of myocardial infarction, coronary revascularization procedures, congestive heart failure, and cardiovascular death. Baseline apnea-hypopnea index was used as the predictor variable in survival analysis models predicting CHD or HF incidence after adjusting for conventional confounders. The incidence of CHD or HF was 10.9 per 1000 person-years; the mean time to event was 11.2 ±5.8 years. After adjusting for age, sex, BMI, and smoking, estimated HR and CI of incident CHD or HF were HR=1.5 (95% CI=0.9 to 2.6) for apnea-hypopnea index >0 to 5; HR=1.9 (95% CI=1.05 to 3.5) for apnea-hypopnea index 5≤15; HR=1.8 (95% CI=0.85 to 4.0) for apnea-hypopnea index 15≤30; and HR=2.6 (95% CI=1.1 to 6.1) for apnea-hypopnea index>30 compared with apnea-hypopnea index=0 (*P* trend=.02). These findings support the hypothesized adverse effects of sleep-disordered breathing on CHD and HF, with individuals with severe untreated obstructive sleep apnea being 2.6 times more likely to have an incidence of CHD or HF than those without sleep-disordered breathing.

Another group[250] presented the importance of sleep-disordered breathing in CVD. Sleep-disordered breathing consists of obstructive sleep apnea and central sleep apnea/Cheyne-Stokes respiration (CSA/CSR). Current evidence suggest that both forms of sleep-disordered breathing, and often a combination of the two, are highly prevalent in patients with a wide variety of CVD, including hypertension, HF, arrhythmias, coronary artery disease (CAD), acute coronary syndrome, and stroke. The existence of sleep-disordered breathing in these patients with cardiac disease is independently associated with worse cardiac function and exercise tolerance, recurrent arrhythmias, infarct expansion, diminished quality of life (QOL), and increased mortality. Recent data suggest positive effects of positive airway pressure (PAP) therapy on QOL and CV function. Moreover, ongoing clinical trials may elucidate the first definitive data for PAP therapy of sleep-disordered breathing on concrete outcomes such as mortality. This review discusses current data accentuating links between sleep-disordered breathing and a multitude of CV conditions, the importance of recognizing and diagnosing sleep-disordered breathing in patients with CVD, and the

impact of effective sleep-disordered breathing treatment on cardiovascular endpoints.

A systematic review[251] examined the impact of obstructive sleep apnea syndrome on patients' occupational health. Nineteen studies were selected that discussed issues related to job performance and productivity, absenteeism, and the psychosocial health of individuals with obstructive sleep apnea syndrome and assessed the risk of bias in their conclusions. The findings suggested the existence of multiple relationships between obstructive sleep apnea syndrome and the work limitations of patients (such as difficulty concentrating, learning new tasks, or performing monotonous tasks); however, these results need to be confirmed by future methodologically rigorous studies. These studies reached more scientifically consistent conclusions about such patients' risk of taking more sick time or having work disability, especially if they reported excessive daytime sleepiness. Very few studies have examined the relationship between obstructive sleep apnea syndrome and psychosocial occupational health of patients. Therefore, more research is needed to clarify these aspects of occupational medicine.

A different review[252] scrutinized the growing information on obstructive sleep apnea and metabolic bone disease. obstructive sleep apnea and low bone mass are 2 prevalent conditions, especially among older adults-a section of the US population that is projected to grow dramatically in the near future. obstructive sleep apnea is the most common form of sleep-disordered breathing and has been linked to numerous cardiovascular, metabolic, hormonal, and inflammatory derangements; it may also have adverse effects on bone. However, little is known about how sleep apnea (including the associated hypoxia and sleep fragmentation) affects bone metabolism. This review examined the information concerning metabolic bone disease and sleep-disordered breathing, and discusses the pathophysiology by which obstructive sleep apnea may affect bone metabolism and architecture.

Another study[253] reviewed the main findings describing the association between stroke and obstructive sleep apnea treatment with CPAP. Sleep-disordered breathing and its relationship to stroke has been a topic of increased interest and research. obstructive sleep apnea is an important risk factor for stroke incidence and mortality; furthermore, obstructive sleep apnea is a common clinical outcome after cerebrovascular accident, directly impacting the patient's recovery. The treatment of choice for obstructive sleep apnea is positive airway pressure, and PAP is regarded as the most recommended clinical management for the treatment of patients with CV complications. However, the implementation of PAP therapy in victims of stroke remains a challenge, considering the increased frequency of motor and language decrements associated with the cerebrovascular accident. The authors review the association between obstructive sleep apnea and stroke, as well as obstructive sleep apnea treatment options, the different options and indications of PAP treatment, PAP adherence, and clinical outcomes following treatment.

A Chinese group[254] examined the impact of obstructive sleep apnea treatment with CPAP on percutaneous coronary intervention (PCI) outcomes. Between 2002 and 2012, the authors identified 390 patients with obstructive sleep apnea who had undergone PCI. Sleep apnea was diagnosed through in-laboratory PSG and defined by an apnea-hypopnea index $\geq$5. The participants were divided into 3 groups: moderate to severe obstructive sleep apnea successfully treated with CPAP (n=128); untreated moderate to severe sleep apnea (n=167); and untreated mild obstructive sleep apnea (n=95). Main outcomes included repeat revascularization, major adverse cardiac events (MACEs, such as death, nonfatal myocardial infarction, repeat revascularization), and major adverse cardiac or cerebrovascular events (MACCEs). The median follow-up interval was 4.8 years. The untreated patients with moderate to severe obstructive sleep apnea had a higher incidence of repeat revascularization than the treated moderate to severe group (25.1% versus 14.1%, P=.019). No differences in mortality (P=.64), MACE (P=.33), and MACCE (P=.76) were found among the groups. When potential confounding variables were adjusted, untreated moderate to severe obstructive sleep apnea was associated with increased risk of repeat revascularization; CPAP treatment reduced this risk.

A retrospective, case-control study[255] sought to assess the cause of ischemic stroke in patients with obstructive sleep apnea compared with controls. Consecutive patients who underwent PSG and had an ischemic stroke within 1 year were identified. Two validated algorithms determined stroke subtype. PSG results were used to sort patients into those with obstructive sleep apnea and controls; CV risk, neuroimaging, and echocardiographic data were also compiled. Fifty-three individuals were evaluated; cardioembolic strokes were more common among those with obstructive sleep apnea than controls (72% versus 33%, respectively; P=.01). The majority of cardioembolic events occurred in those with moderate to severe obstructive sleep apnea. Atrial fibrillation (AFib) was also more frequent in patients with sleep-disordered breathing (59% versus 24%, respectively; P=.01). The association between cardioembolic stroke and obstructive sleep apnea remained significant after controlling for AFib (P=.03; OR=4.5). The authors conclude that a high rate of occult paroxysmal AFib in this obstructive sleep apnea population may exist; also, obstructive sleep apnea may lead to cardioembolic strokes through mechanisms independent of AFib.

A different study[256] explored the association between glucose metabolism and sleep-disordered breathing based on sleep stage. Sleep-disordered breathing is associated with impaired glucose metabolism; rapid eye movement (REM) versus non-REM stages may show differences in the uptake of glucose due to sleep-state-dependent sympathetic activation and/or level of hypoxemia. A cross-sectional analysis of a community-based sample included 3310 participants from the Sleep Heart Health Study (53% women; mean 66.1 years of age). Full-channel home PSG and fasting glucose were available for all individuals. Sleep-disordered breathing severity during REM and NREM was quantified using the apnea-hypopnea index in REM and NREM, respectively. Fasting and 2-hour postchallenge glucose levels were measured during a glucose tolerance test in 2264 participants; the HOMA-IR was determined in 1543 participants. apnea-hypopnea index REM and apnea-hypopnea index NREM were associated with fasting glycemia, postprandial glucose levels, and HOMA-IR in models adjusted for age, sex, race, and site. With further adjustment for BMI, waist circumference, and sleep duration, apnea-hypopnea index REM was found to associate only with HOMA-IR, whereas apnea-hypopnea index NREM was associated only with fasting and postprandial glucose levels. The researchers concluded that apnea-hypopnea index in REM sleep is associated with insulin resistance but not with fasting glycemia or glucose intolerance.

A large population-based, multicenter, prospective study[257] evaluated sleep-disordered breathing indices as predictors of incident atrial fibrillation. Existing research supports an association between sleep-disordered breathing and AFib; however, prospective data examining sleep-disordered breathing as predictive of incident AFib are lacking. A cohort of 843 ambulatory older men without prevalent AFib was tested for baseline sleep indices: apnea-hypopnea index, central sleep apnea, central apnea index ≥5 versus <5), central sleep index or Cheyne-Stokes respiration, obstructive apnea-hypopnea index, and percentage of sleep time with <90% oxygen saturation. Incident clinically symptomatic adjudicated or self-reported AFib outcome was determined (mean follow-up 6.5 ±0.7 years). Logistic regression models were adjusted for age, race, BMI, cardiopulmonary disease, alcohol use, pacemaker, cholesterol level, cardiac medication, and alternate apnea type for obstructive and central apnea; age interaction terms and median age-stratified analyses were performed. CSA (OR=2.58; 95% CI=1.18 to 5.66) and CSA-CSR (OR=2.27; 95% CI=1.13 to 4.56), but not obstructive apnea or hypoxemia, predicted incident AFib. Central apnea, Cheyne-Stokes, and sleep-disordered breathing-age interaction terms were significant ($P<.05$). Atrial fibrillation was related to central apnea (OR=9.97; 95% CI=2.72 to 36.50), central apnea-CSR (OR 6.31; 95% CI=19.4 to 20.51), and apnea-hypopnea index (OR=1.22; 95% CI=1.08 to 1.39 per 5 unit increase) among participants ≥76 years of age compared with younger individuals. The authors concluded that in older males, CSA and CSR predicted increased AFib risk with findings stronger in older patients in whom overall sleep-disordered breathing also increased atrial fibrillation risk.

Another Chinese group[258] gathered evidence from a large-scale cross-sectional study dealing with the association of elevated low-density lipoprotein (LDL) and obstructive sleep apnea. Lipid metabolism disorder is acknowledged to be associated with obstructive sleep apnea, but inconsistent results have been reported. This project sought to evaluate the association between lipid profile and sleep apnea with adjustments for multiple confounders. Participants (total=2983) were recruited from the Shanghai Sleep Health Study between 2007 and 2013. Data gathered included overnight PSG markers, serum lipids, fasting blood glucose, insulin levels, and anthropometric measurements. Multivariate logistic regression analyses were used to determine the correlation between lipid profile and obstructive sleep apnea with adjustments for variables including lipids, age, sex, Epworth sleepiness scale, BMI, waist-to-hip ratio, glucose, insulin resistance, hypertension, and smoking. The prevalence of hyper total cholesterol, hypertriglycerides, hypo high-density lipoprotein (HDL) cholesterol, hyperLDL, hyperapolipoprotein A to I (apoA-I) and hyperapoB differed markedly between the patients without obstructive sleep apnea and sleep apnea. Without considering the interaction across different lipids, total cholesterol, LDL, and apoB were independently associated with obstructive sleep apnea in primary multivariate logistic regression analyses (OR=1.262; 95% CI=1.109 to 1.438; OR=1.432; 95% CI=1.233 to 1.664; and OR=5.582; 95% CI=2.643 to 11.787, respectively). Only LDL was found to be an independent risk factor for obstructive sleep apnea (OR=1.430; 95% CI=1.221 to 1.675) in further analyses. The authors concluded that they demonstrated that patients with obstructive sleep apnea had a higher percentage of dyslipidemia than those without obstructive sleep apnea; LDL was the only component of serum lipid that was demonstrated an independent association.

A separate study[259] investigated whether self-reported obstructive sleep apnea, simple snoring, and various markers of sleep-disordered breathing were associated with CV risk. A representative nationwide cohort of 5177 Finnish adults ≥30 years of age was evaluated. The participants were measured for conventional CV risk factors and responded to sleep-disordered breathing-related questions derived from the Basic Nordic Sleep Questionnaire, which were used to operationalize self-reported obstructive sleep apnea. The

primary endpoint was incidence of a CV event (CV mortality, nonfatal MI, nonfatal stroke, hospitalization for HF, or coronary interventions). During a median follow-up of 11.2 years (52 910 person-years), 634 participants experienced a CV event. In multivariate-adjusted Cox models, self-reported obstructive sleep apnea (HR =1.34; 95% CI=1.04 to 1.73; *P*=0.03) was an independent predictor of cardiovascular events. Self-reported simple snoring by itself was not found to be associated with future cardiovascular events; however, among snorers (n=3152), frequent breathing cessations and very loud and irregular snoring were associated with cardiovascular risk. The researchers concluded that self-reported obstructive sleep apnea and sleep-disordered breathing-related snoring variables are associated with CV risk, whereas simple snoring is not. They recommend that questions in clinical practice and on surveys concerning habitual snoring should be amended with questions addressing respiratory pauses and stertorous snoring, which can be used to estimate the risk of obstructive sleep apnea and cardiovascular events.

A community dwelling cohort[260] was recruited to examine the relationship between obstructive sleep apnea and high-sensitivity troponin T (hs-TnT), cardiac structure, and CV outcomes based on sex. A cohort of 752 men and 893 women free of CVD participating in both the Atherosclerosis Risk in the Communities (ARIC) and the Sleep Heart Health Study (SHHS) were included. All participants (mean 62.5 ±5.5 years of age) underwent PSG and measurement of hs-TnT. Sleep apnea severity was defined using established clinical categories. Participants were followed for 13.6 ±3.2 years for incident coronary disease, HF, and CV and all-cause mortality. Surviving individuals underwent echocardiography after 15.2 ±0.8 years. Obstructive sleep apnea was independently associated with hs-TnT among women (*P*=.03) but not in men (*P*=.94). Obstructive sleep apnea was also independently associated with incident HF or death in women (*P*=.03) but not men (*P*=.10). This association was no longer significant when adjusting for hs-TnT (*P*=.09). Among surviving individuals without an incident cardiovascular event, obstructive sleep apnea assessed in midlife was independently associated with greater left ventricle mass index only among women (*P*=.001).

A systematic review and meta-analysis by Chinese investigators[261] explored sexual dysfunction in patients with obstructive sleep apnea. Epidemiologic findings are inconclusive regarding the risk for sexual dysfunction related to sleep apnea. PubMed, Cochrane Library, and Embase databases were searched for observational studies on obstructive sleep apnea and the risk of sexual dysfunction. The quality of the methods of the case-control and cohort studies was assessed using the Newcastle-Ottawa Scale (NOS). The cross-sectional quality study quality methodology checklist was used for cross-sectional study. Data were pooled for the random-effects model. Sensitivity analyses were conducted to assess potential bias. This analysis consisted of 1275 participants from 9 studies. Five studies reported the incidence of erectile dysfunction (ED); the remaining 4 studies reported the incidence of female sexual dysfunction (FSD). Pooled results showed that obstructive sleep apnea was associated with elevated risk of ED (pooled RR=1.82, 95% CI=1.12 to 2.97) as well as FSD (pooled RR=2.00; 95% CI=1.29 to 3.08). Estimates of the total effects were found to be generally consistent in the sensitivity analysis. No signs of publication bias were observed. They call for more research to clarify the relationship between obstructive sleep apnea and the increased risk of sexual dysfunction.

Sleep bruxism and temporomandibular disorders

A Canadian review[262] updated the current status of sleep bruxism (SB) in the practice of respiratory medicine. SB consists of involuntary episodic and repetitive jaw muscle activity characterized by occasional tooth grinding or jaw clenching during sleep. Prevalence is between14% and 20% in childhood and drops to between 3% and 8% in adults. The causes and mechanisms of idiopathic-primary sleep bruxism are unknown; however, putative possibilities include psychological risk factors (such as anxiety, stress due to life events, and hypervigilance) and sleep physiological reactivity (for example, sleep arousal associated with autonomic activity and/or respiratory events). Neurotransmitters including serotonin, dopamine, noradrenaline, and histamine have been proposed to play an indirect role in SB; however, their exact role in rhythmic masticatory muscle activity (RMMA; the electromyographic hallmark of SB) genesis remains unknown. No specific gene is associated with SB, and familial environmental factors play a substantial role. At the time of this review, no single explanation has accounted for the SB mechanism. Secondary SB with sleep comorbidities that should be clinically assessed includes insomnia, periodic limb movements, sleep-disordered breathing, gastroesophageal reflux disease, and neurologic conditions (including sleep epilepsy and REM sleep behavior disorder). SB is objectively quantified by scoring RMMA events in parallel with brain, respiratory, and cardiac activity using in-laboratory or home PSG. More precise diagnostic accuracy arises with the use of audio-video recordings in conjunction with the laboratory sleep test in the presence of neurological conditions. The authors maintain that management strategy should be customized to the patient's phenotype and comorbidities; in the presence of sleep-disordered breathing, a mandibular advancement device or CPAP is preferred over single occlusal splint therapy on the maxilla.

Another review[263] provides an expert opinion on the possible temporal relationships between sleep bruxism and obstructive sleep apnea events. SB covers different motor phenomena with various risk and etiological factors and possibly different clinical relevance, especially as far as it may protect against obstructive sleep apnea. Four hypothetical scenarios for a temporal relationship may be classified: (1) the 2 phenomena are unrelated; (2) the onset of the obstructive sleep apnea event precedes the onset of the sleep bruxism event within a limited time span, with SB having a potential protective role against apneic events; (3) the onset of the bruxism event precedes the onset of the sleep apnea event within a limited time frame, with SB having an obstructive sleep apnea-inducing effect; and (4) the onset of the obstructive sleep apnea and SB events occurs at the same instant. Findings on this relationship are inconclusive; the authors hypothesized that all of the aforementioned scenarios are plausible and that the predominance of one specific sequence of events varies from individual to individual. SB may be protective against obstructive sleep apnea by protruding the mandible and restoring airway patency. They conclude that the SB-obstructive sleep apnea relationship is complex and individual differences may explain the different sleep bruxism-sleep apnea relationships, especially in regards to the specific anatomic site of obstruction.

A different Canadian study[264] examined the relationship between RMMA in SB and transient hypoxia in the absence of sleep-disordered breathing. SB activity is characterized by RMMA; many but not all episodes of RMMA are associated with sleep arousal. Sleep laboratory or home sleep testing data from 22 SB (tooth grinding history in the absence of reported sleep-disordered breathing) and healthy participants were examined. A total of 143 RMMA/SB episodes were classified in 4 categories: no arousal and no body movement; arousal and no body movement; no arousal and body movement; arousal and body movement. Blood oxygen saturation (SaO_2) was assessed from finger oximetry signals at baseline (that is, before RMMA) and during RMMA. Significant variation in SaO_2 over time was found after RMMA onset (+7 to +9 seconds). No differences between categories and no interactions between categories and SaO_2 variations over time were observed. Oxygen saturation in 6 of 22 participants (27%) remained equal or increased slightly after the RMMA/SB onset (+8 seconds) compared with baseline; 10 individuals (45%) slightly decreased (a drop of 0.01-1%) and the remaining (27%) decreased between 1 and 2%. These results suggest that a subset of SB participants had a minor transient hypoxia potentially associated with the onset of RMMA episodes, which occurred independently of concomitant sleep arousal or body movements.

Another study[265] sought to determine an appropriate cutoff value and the number of nights of sleep with a portable single-channel electromyographic (EMG) device necessary for a valid sleep bruxism diagnosis. Twenty consecutive postgraduate students and staff at a Brazilian dental school enrolled in the study. Each participant underwent the testing for 5 consecutive nights and polysomnography. The discrimination between bruxers and nonbruxers relied solely on PSG. Data about EMG per hour with the device and PSG (bursts per hour) were recorded. There were positive correlations between the device and the sleep laboratory test for EMG/hour and bursts/hour in 3 and 5 consecutive nights. Bland-Altman analysis of the EMG bursts per hour showed positive agreement between the methods. Receiver operating characteristic analyses also demonstrated that using a minimum of 18 EMG per hour for 3 nights and 19 EMG per hour for 5 nights in the device as cutoffs resulted in a 90% specificity and positive likelihood ratio=5. They conclude that the device studied may be a valid choice in clinical practice for SB assessment when used for 3 or 5 nights of recording and is able to recognize sleep bruxism diagnosed by the gold standard of PSG.

A different project[266] also investigated single-channel EMG recordings for assessment of SB by attempting to evaluate an EMG algorithm in comparison with PSG testing. Sleep laboratory testing data from 20 participants with different frequencies of jaw-muscle EMG activity were analyzed using the GS algorithm, including previously published criteria for EMG analyses and contrasted with 2 different algorithms. One was based on a signal recognition algorithm and the other on a moving average estimation method, which is a comparison of the EMG amplitude with the estimated background level; the rules for detection of RMMA are then applied. The greatest correlation coefficients (r=.96) were obtained between the GS and the moving average algorithm; however, no substantial differences were found in the absolute numbers of EMG bursts between the signal recognition and moving average algorithms during sleep. When awakenings during sleep were included in the analyses, both algorithms significantly overestimated the EMG bursts. No major differences were noted between right and left sides or muscles. The authors conclude that a moving average algorithm may be useful for assessing EMG activity during sleep but with recognition of the possible overestimation of EMG activity due to transient awakenings.

A German group[267] explored sleep-associated aspects of TMD with myofascial pain in the orofacial area of patients and controls. A total of 305 female patients were screened to select 44 participants fulfilling the inclusion criteria, 22 experiencing myofascial pain and 22 as controls. Sleep quality was evaluated by use of the Pittsburgh Sleep-Quality-Index (PSQI) and a validated German

sleep questionnaire (SF-AR). Tooth wear was measured, and anterior temporalis muscle activity was assessed at home for several nights with a portable EMG device. The 22 patients were 45.0 ±13.6 years of age; the 22 controls were 45.2 ±9.0 years of age. The PSQI score was 7.5 ±3.7 for patients and 4.4 ±3.0 for the control group (P=.006). The SF-AR demonstrated that 23% of the controls and 14% of the patients were "long sleepers." The overall number of episodes in the 2 groups was not substantially different (4.10 ±2.65 versus 4.57 ±1.99 episodes per hour, respectively). However, more of the pain group had temporalis activity possibly related to SB during all 4 consecutive nights (P=.04). Based on definitions from the International Classification of Sleep Disorders, 3rd edition, 13.6% of the controls and 71.4% of the patients (P<.001) exhibited SB. The authors concluded that sleep-associated disturbances, including reduction of sleep quality and increased prevalence of SB and facial pain in the morning, occurred substantially more often among patients with TMD. SB varied over the nights especially in the control group. This should be accounted for when the prevalence of SB is assessed with EMG.

CARIOLOGY

The literature on dental caries in 2015 progressed, as it has in the past decade, with an increased number of research articles and reports compared with the previous year. Among the published data, after a selective screening for RCTs, only 8 papers were selected and further analyzed. Two studies were excluded after careful examination and only 6 articles were kept for further review. Besides the RCTs, the main topics covered were demographics, which numerically represents the largest portion of articles published on caries but did not add any knowledge on the comprehension or possibility of treatment of this disease. However, 1 study from Norway [268] of a large number of patients followed longitudinally for 10 years on a broad spectrum of population deserves mention. The study reported a significant reduction in the number of carious teeth from 2003 to 2012, indicating a trend that could probably be seen in most industrial countries such as Norway. Genetic/biomolecular studies were also extensively published and added important new information on the path to full comprehension of the mechanism behind the formation of dental biofilms and antibacterial strategies varying from selective mechanism, to mouthrinses, to dental materials with intrinsic antibacterial properties. While waiting for a definitive treatment against caries, prevention remains the only effective solution against dental caries and this subject was covered extensively in the literature in 2015. Numerous articles were also published on the diagnosis of caries and the remineralization of carious dental tissue.

Randomized controlled trials

Probiotics are defined as live microorganisms that benefit the health of the host when administrated in correct quantities. Two RCTs published in 2015examined the efficacy of probiotics against dental caries. The first paper[269] compared, in a randomized double-blind placebo-controlled study, 138 healthy 2- to 3-year-old children living in a low socioeconomic multicultural area divided into 2 groups. The test group chewed a probiotic tablet regularly, and the control group chewed an identical tablet with no probiotics. The parents of both groups were instructed to brush their children's teeth twice a day with fluoride toothpaste. The caries increment was significantly lower in the test group compared with that in the controls, meaning that early childhood caries development could be reduced by administering these probiotic-chewing tablets as an adjunct to the daily use of fluoride toothpaste in preschool children.

The second RCT was every child's dream and offered the chance of reducing caries risk with an ice-cream.[270] Sixty children randomly divided into 2 groups were followed for 6 months. The test and control group received ice-cream with and without probiotics for 7 days, and their *S. mutans* levels in saliva samples were calculated and compared with baseline at 7 and 30 days and 6 months. Probiotic ice-cream significantly reduced the *S. mutans* count after 7 days and also after a 30-day washout period, whereas normal ice-cream consumption resulted in no significant reduction. After 6 months, the salivary levels of *S. mutans* were similar to those at baseline. in both groups. This means, in accordance with previous research, that probiotics must be ingested regularly and not discontinued in order to maintain their beneficial effect.

Two RCTs evaluated the remineralization potential of early carious lesions. The first study,[271] although on a limited number of only 13 participants, compared the efficacy of casein phosphopeptide-stabilized amorphous calcium phosphate complexes (CPP-ACP)-containing cream (without fluoride) after the use of fluoride toothpaste with the prolonged use of fluoride toothpaste or brushing with no fluoride toothpaste on enamel caries lesions in situ using removable appliances and bovine demineralized enamel in 2 different sites in the mouth. One site was more cleansable and one more difficult to access. The conclusion of the study was that the extended use of fluoride-containing toothpaste enhanced remineralization significantly in both the potentially influencing factors (brushing and position) under investigation. In contrast, CPP-ACP-containing cream with no fluoride showed little beneficial effect in enhancing remineralization. Especially for plaque-retaining areas, CPP-ACP appears to impede the remineralizing process induced by the use of fluoride toothpaste.

The second study of remineralization[272] aimed to evaluate the effects of novel CPP formulations. These formulations were CCP-ACP, and CPP-amorphous calcium fluoride phosphate (CPP-ACFP) versus fluoride varnish on the remineralization of enamel white spot lesions over a 12-week follow-up period. This double-blind prospective study compared 786 white spot lesions randomly divided into 3 groups: the first group used daily CCP- ACP, the second group used CPP-ACFP, and the third group received a monthly application of fluoride varnish. To compare the efficacy of the different treatments, both the International Caries Detection and Assessment System (ICDAS II) and laser fluorescence (DIAGNOdent) were used at baseline and at 4, 8, and 12 weeks. Although CPP-ACFP seemed to have a specific effect on smooth-surface caries but no significant effect on caries in pits and fissures, it could be concluded that, at 4 weeks, CPP-ACFP was better than fluoride varnish at remineralizing smooth surface white spot lesions. CPP-ACP was not better than fluoride varnish by any of the measurements studied.

The next RCT[273] compared the 24-month survival of composite resin restorations in primary molars after partial caries removal and total caries removal. Forty-eight children 3 to 8 years of age with at least 1 deep carious lesion were included in the study, with a total of 120 teeth. For PCR, excavation was stopped when dentin with a leathery consistency was found; in the total caries removal group, the total absence of carious tissue was confirmed using a dull-tipped explorer. Pulpotomy was completed in patients with pulp exposure. Success was measured by modified USPHS criteria with Alfa and Bravo scores recorded as success. If pulp exposure (that occurred in 15 teeth in the total caries removal group) and restoration failure (that was higher in the partial caries removal group compared with the total caries removal group with 34% versus 14%, respectively) were considered as the outcome, there were no significant differences between the 2 groups with success rates of 64% (partial caries removal) and 61% (total caries removal). Deciduous teeth submitted to partial caries removal prevented pulp exposure and, consequently, more invasive treatments; otherwise, partial caries removal yielded lower longevity for composite restoration compared with total caries removal, suggesting that partial caries removal restorations need to be followed over time, especially when multisurface restorations are involved.

Finally the last RCT, by Lee et al,[28] reported that xylitol consumption did not offer additional benefit beyond other preventive measures represented by oral health education, toothbrushing and fluoridated toothpaste, topical fluoride varnish treatment, and dental sealants. Caries progression in the permanent teeth of both groups was minimal, suggesting that other simultaneous prevention modalities may have masked the possible beneficial effects of xylitol in this trial.

Genetic/biomolecular studies

Specifically targeted antimicrobial peptides (STAMPs) are very small peptides made of a few amino acids able to selectively kill specific bacterial microorganisms. A paper publish by Guo et al[274] tested the efficacy of a STAMP (C16G2) engineered against *S. mutans* versus 20 different bacterial species in monoculture, including both oral and nonoral Gram-positive and Gram-negative species. To further test the selective antimicrobial activity of C16G2 against *S. mutans* in a multispecies community of biological relevance, an *S. mutans*-infected multispecies oral microbial community was artificially obtained by adding JM11, a spectinomycin-resistant *S. mutans* strain, to a saliva-derived, SHI medium-cultivated planktonic culture. The main purpose of the study was to verify what happens to the bacterial community when a particular bacterium is selectively killed. Interestingly, a significant shift in the community variety and relative abundance of various *Streptococcus* spp was discovered by metagenomic analysis. Bacteria within the same biofilm showed wide and complex interactions, such as competition between bacteria for nutrients, synergistic/mutualistic interactions, which may stimulate the growth or survival of one or more residents, and production of an antagonist by one resident, which inhibits the growth of another. Therefore, the selective killing of one or a few community members could potentially affect many bacterial species and result in a complete shift of the microbial composition within the community. The authors reported that the reduction in *S. mutans* population was accompanied by an increase in *Streptococcus mitis*, which is among the most prevalent bacterial species detected in the oral cavity of healthy humans. At the same time, pathogens such as *Veillonella*, were drastically reduced while *Fusobacterium periodonticum* and *Campylobacter*, *Gemella*, and *Neisseria* organisms could not be detected after treatment with C16G2. The ability of targeted antimicrobial peptide technology to target specific bacterial species within the multispecies community could, therefore, be used for investigating the potential roles of specific bacterial species in maintaining the stability of the community as well as contributing to community-associated physiology and pathogenicity. Furthermore, after the recent progress of metagenomic[275] and metaproteomic[276] studies demonstrating that many more bacterial species are involved in biofilm formation, development, and stability than previously thought, it is clear that the most appropriate approach to caries treatment must be aimed at shifting the biofilm toward a healthy state instead of trying to hamper its inevitable formation.

Dental caries is intimately linked to pH dynamics. In supragingival plaque, after the addition of a carbohydrate

source, bacterial metabolism decreases the pH. and there is a shift of the bacterial community toward more cariogenic bacteria that are acidogenic and acid-tolerant. Most scientists believe in the so called "ecological plaque hypothesis," according to which, when the low pH is reached, a homeostatic mechanism is responsible for regulating the pH back to neutral.[277] Implicit in these concepts is the idea that disease can be prevented not only by directly inhibiting acidogenic and aciduric caries-associated pathogens but also by interfering with the environmental factors driving the selection and enrichment of these bacteria. In addition, endogenous and biofilm related factors that help in re-establishing a neutral pH is a second approach in combatting the disease. Molecular mechanisms supporting this important homeostasis are poorly characterized mainly because there are hundreds of active species in dental plaque.

Using a double approach of sampling for mRNA (metatranscriptomics) and metabolites (metabolomics) during the pH drop and recovery, Edlund et al,[278] in one of the most important papers published on dental caries in 2015, reported a full dataset producing new insights into the species and activities that influence this fundamental homeostatic process. This well-designed and scientifically rigorous research performed the first full transcriptome and metabolome analysis of a diverse oral plaque community by using a functionally and taxonomically robust in vitro model system with more than 100 species. Differential gene expression analyses from the complete transcriptome of 14 key community members revealed highly varied regulation of both known and previously unassociated pH-neutralizing pathways as a response to the pH drop. Unique expression and metabolite signatures from 400 detected metabolites were found for each stage along the pH curve, suggesting it may be possible to define healthy and diseased states of activity. Importantly, to keep a healthy plaque pH, gene transcription activity of known and previously unrecognized pH-neutralizing pathways was associated with the *Lactobacillus*, *Veillonella*, and *Streptococcus* genera during the pH recovery phase. For the first time, the authors demonstrated that their in vitro model allows the study of changes in key metabolic processes like carbohydrate utilization, pH stress, and pH recovery in an environment with a very complex microbiological community. More importantly, they identified some critical metabolic activities that are probably key for health-associated pH recovery, which could also be related to poorly studied species (for example, *Veillonella* spp). This study represents a starting point for defining healthy and disease-like states when sampling the metabolome or transcriptome of the highly variable supragingival plaque of human populations.

Regarding the role of lactobacilli in caries, another paper, by Caufield et al,[279] firmly proposed the hypothesis, in accordance with their research, that lactobacilli are opportunistic invaders of precaries or existing carious lesions, rather than members of the indigenous microbiota that naturally coexist with the human host. Unlike most saprophytic microbes that stably colonize a host, lactobacilli appear to be planktonic, opportunistic colonizers that are able to group and grow only in certain restrictive niches of the host, at least within the oral cavity. The authors postulated that to have a sustained colonization of lactobacilli in humans, 3 essential requirements are necessary: first a stagnant, retentive niche that is mostly anaerobic; second a low pH milieu; and third the possibility of having ready access to carbohydrates. Because only 3 sites on the human body meet these requirements, carious lesions, the stomach, and the vagina, and because only a handful of *Lactobacillus* spp are found in carious lesions, they are largely absent in caries-free children. It seems that lactobacilli present in carious lesions represent both a major contributor to caries progression and, at the same time, a major reservoir for the gastrointestinal tract.

Among the various types of streptococci present in the oral cavity, one particular strain deserves attention, the nutritionally variant *Streptococcus* (NVS). An interesting paper from Italy tested the competition between NVS and *S. mutans*.[280] Although it was an in vitro study and the competitive effect was tested on a glass surface and on hydroxyapatite, NVS were able to compete with *S. mutans* because of higher hydrophobicity (NVS organisms are more efficient than *S. mutans* in binding to glass surfaces in a competition for space) and because the production of a large number of cell-wall lytic enzymes by NVS can cause a biochemical modification of *S. mutans* adhesion factors.

Moreover, NVS were able to interfere with *S. mutans* adhesion to glass even when they were added to the culture several hours after the growth of *S. mutans* on the glass surface. This indicates that, in some way, NVS were even able to disengage *S. mutans* cells when they were already attached to hard surfaces. To date, no information is available on the role of bacteriolytic enzymes on NVS physiology and reproduction, but the potential clinical implication of this line of research seems very promising.

One of the human body's most useful defense mechanisms on wet epithelial linings such as the mouth, gastrointestinal tract, and lungs is a coating of abundant, well-hydrated mucus. The main constituent of mucus are mucins, large glycoproteins that play a fundamental role in maintaining a healthy microbial environment. Defects in mucin production are associated with diseases such as ulcerative colitis when mucins are underproduced or cystic fibrosis and asthma when mucins are produced in excess. In addition, studies have shown that mucins can interact with microbes such as *Helicobacter pylori*,

Haemophilus parainfluenzae, and human immunodeficiency virus.[281] Frenkel and Ribbeck[282] explored the connection between purified human MUC5B and the virulence of *S. mutans*. They determined that MUC5B does not alter *S. mutans* growth or lead to bacterial killing over 24 hours but limits biofilm formation by maintaining *S. mutans* primarily in the planktonic form. They speculated that the reported reduction in bacterial attachment and biofilm formation is the consequence of a combination of genetic changes that decrease bacterial virulence and repulsion by MUC5B's heterogeneous glycans.

S. mutans attachment and biofilm formation are critical phases in the development of caries, therefore, these results are particularly important from a clinical point of view. The presence or absence of MUC5B in the mouth could modify the individuals' susceptibility to caries and then be an easily accessible, highly predictable clinical diagnostic marker of disease. In addition, from a therapeutic standpoint, exogenous MUC5B could theoretically be used as treatment or prevention of caries. A direct correlation has also been demonstrated between saliva Proteinase 3 and the severity of dental caries as indicated by the negative relationship between salivary PR3 concentration, the severity of caries, and the susceptibility of *S. mutans* to PR3.[283]

In conclusion, in caries formation and development, we now know things are much more complex that we thought,[275,276] as many more bacteria are involved and become active in the biofilm at different pH stages; some of them are trying to keep the pH low, some of them trying to bring it back to neutral.[284] However, it seems that *S. mutans* is still critical for the initiation of the biofilm formation and initial pH drop, and if *S. mutans* is present, caries will progress, meaning the acidogenic bacteria will prevail. If *S. mutans* is not present, all the bacteria that work in favor of a higher pH will tend to prevail.[274] Endogenous factors like mucins seem to have a critical role in protecting against caries formation, and the antagonistic effect of other microbiota can be also used to contrast the role of key bacteria like *S. mutans* in caries formation. The final goal, ultimately, is to promote an ecological shift of the biofilm toward its healthy state as described by Takahashi.[284] This is a "must read" review for readers interested in how oral microbe metabolism functions.

Diagnosis/prevention/remineralization

Because dental caries is the most wide spread disease in humans, finding the most efficient way to diagnose it remains a fundamental goal of many clinician and researchers. Several methods have been proposed to identify dental caries, ranging from visual and tactile examination and radiographs to fiber-optic transillumination (FOTI), Diagnodent (DD), electronic caries monitor (ECM) and quantitative light-induced fluorescence (QLF). A thorough systematic review by Pretty and Ekstrand[285] on this topic concluded that the current evidence base suggests that, while there are various devices or technology-enabled detection systems, the use of a careful, methodical visual inspection of clean, dry teeth, supplemented, where indicated by radiographic views remains the standard of care in caries detection and diagnostics. It is expected that a single method, with a single "mode of action" fails to reach the diagnostic performance of a clinical examination undertaken by a trained clinician who can combine the detection and diagnosis processes into a single process.[286] Similarly, a systematic review on diagnosis of secondary caries by Brouwer et al[287] failed to identify a single method to identify these types of lesions and concluded that all methods can be useful but none is adequate alone. If tactile/visual examination must be accompanied by a radiographic examination to have the highest degree of predictability, radiographs alone are highly predictable only in cavitated proximal lesion and dentinal caries.[288] Today, not all carious lesions must necessarily be treated clinically but various methods of promoting remineralization can be used. In these patients, existing visible and radiographic systems nay be used to monitor lesions over time.

Using low-cost intraoral cameras facilitates the recording of lesion appearance in the patient record and may be of significant benefit in monitoring early lesions over time after detection. This benefit extends to the clinician and the patient for whom it may be a useful educational and motivational tool. A new method has also been proposed,[289] using only occlusal intraoral photographs and a fully automated caries diagnostic system as a low-cost additional diagnostic tool.

Until a definitive effective treatment against dental caries is found, prevention still remains the most reliable clinical approach. For this purpose mouth-rinses are often prescribed by dental clinicians to their patients as an important aid for prevention. Although effective chlorhexidine based mouth rinses are still not indicated for regular usage in their most active concentration, mouth rinses based on essential oils are widely used by patients. In a systematic review by Freires et al,[290] the antibacterial activity of essential oils against cariogenic bacteria was analyzed. Essential oils extracted from a range of aromatic plants worldwide can be considered promising fonts of bioactive products effective against caries-related microorganisms, particularly *S. mutans*; however, most of the dental literature is founded on in vitro studies and on a limited number of clinical trials. Generally, the studies have evaluated the effects of essential oils and isolated compounds on microbial growth rather than virulence factors, which play a

strategic role in the etiopathogenesis of dental caries. Attention is also drawn to the fact that several studies do not offer any chemical or botanical detailed data, raising concern about the reproducibility and accuracy of their results. The authors concluded their review with the comment that scientific journals should be more stringent in the adoption of criteria for the publication of studies with natural products.

The presence of carbohydrates is an essential requirement for caries formation. Because of this, an important part of research is finding the right substitute for sucrose among those sugars that for some reasons are not metabolized by *S. mutans* and other cariogenic bacteria. Among these xylitol has been widely studied, as previously mentioned[28] and many papers are supporting its regular use as a preventive aid against dental caries. For this reason its use has been proposed not only for its regular use as a sugar but also in other products as preventive aids. However, Riley et al[291] found some low quality evidence to suggest that fluoride toothpaste containing xylitol may be more effective than fluoride-only toothpaste for preventing caries in the permanent teeth of children, and that there are no associated adverse-effects from such toothpastes. This does not necessarily mean that xylitol is effective against dental caries but simply that more well-designed studies are needed to prove this concept. Recently also a new polyol, arabitol, isomer of xylitol, has been proposed as an alternative to sucrose. This sugar was tested in laboratory research, in its antibacterial capacity against *S. mutans* and *Lactobacillus* and found to be equally effective as xylitol.[292] Given less expensive arabitol production by yeast fermentation, the finding of this study could open up a new opportunity for prevention of dental caries.

When caries prevention is the topic, fluoride is usually the main character. In a short, not systematic, although very useful review all the various fluoride containing agents that are clinically effective in arresting progression of carious lesions are summarized.[293] Twenty-one papers were included in the review after initial screening. The conclusion of the review was that silver diamine fluoride analyzed in 10 of 21 papers is a straightforward and low-cost method with caries arresting properties, successful at semiannual application at 38% concentration, with most studies performed on primary teeth. Fluoride varnish treatment effectively inhibits demineralization, resulting in highly significant caries reductions while arginine with an insoluble calcium compound in dentifrices has the potential to arrest and reverse dental caries lesions. On the contrary in dentin caries of preschool children Duangthip et al[13] reported that there is limited evidence to support the effectiveness of SDF applications or daily tooth brushing with fluoride toothpaste in arresting or slowing down the progression of active dentin caries in primary teeth. More well-designed randomized controlled trials are required to confirm these findings.

In addition to fluoride, research scientists have also investigated other agents which could be of value in helping the dental team and their patients to control dental caries. Among these, casein phosphopeptide, amorphous calcium phosphate (CPP-ACP) and the new casein phosphopeptide, amorphous calcium phosphate with fluoride (CPP-ACPF) have attained great popularity. CPP is a milk-derived protein able to bind calcium and phosphate ions and stabilize them as ACP. CPP-ACP adheres in the mouth to plaque pellicle, hydroxyapatite, as well as soft tissues. It provides bioavailable calcium and phosphate into saliva, allowing it to drive remineralization. In vitro studies show that when placed on a tooth surface, CPP-ACP interacts with hydrogen ions and is able to diffuse into enamel where it yields to subsurface mineral gains. When dentists recommend products for clinical use, there must be sound scientific evidence to support their application. The manufacturer's instructions recommend CPP-ACP for patients of any age, except for those with milk protein allergies, but limits the indication of CPP-ACPF to patients over 6 years of age because of the fluoride content. These products are much more expensive than any fluoride products, so evidence supporting their general usage is essential. A rigorous systematic review by Raphael and Blinkhorn[294] tried to answer this question "is there sufficient clinical evidence available to support the use of these products over a routine oral care regimen for the prevention and treatment of early dental caries?" Only 12 studies met the inclusion criteria and were selected for final analysis. The findings of this systematic review suggest a lack of evidence to support the use of both CPP-ACP and CPP-ACPF over a routine preventive fluoride regimen for the prevention of early dental caries. With regard to the use of CPP-ACP and CPP-ACPF for the regression of white spot lesions associated with orthodontic treatment, their use might be beneficial, but the quality of evidence is limited. Moreover, presently, support for the use of the fluoride-containing formulation over the CPP-ACP is absent. New products require clinical testing over time, and the absence of adequate high level clinical evidence for the efficacy of these specific casein phosphopeptide amorphous calcium phosphate-containing products is problematic. Further well-designed randomized controlled trials are required before recommending CPP-ACP and CPP-ACPF for the prevention and treatment of early dental caries in the general population.

A research paper by Padovano et al[295] tested whether dentin matrix protein I (DMPI), a noncollagenous calcium-binding protein that plays a critical role in biomineralization, could be used for dentin remineralization.

The study involved testing the efficacy of the peptides to bind collagen of fully demineralized, native and collagenase-challenged, human dentin and investigating the HA nucleation and growth process within the dentin matrix using a solution containing physiological levels of calcium and phosphate.

This study proves that synthetic peptides derived from DMP1 bind type I collagen and promote nucleation of HA within native and collagenase-challenged demineralized dentin substrates when exposed to physiological concentrations of calcium and phosphate ions in vitro. In summary, the study concluded that synthetic polypeptides derived from DMP1 are capable of binding demineralized human dentin. In addition, these peptides can stabilize nucleation clusters from physiological levels of calcium and phosphate. Also, an ideal ratio of these peptides results in HA formation utilizing both calcium-binding domains found in endogenous DMP1. Finally, the ideal ratio of these peptides effectively promotes hydroxyapatite formation within native and collagenase-challenged dentin matrices within a short period of exposure. The authors, with all the limitations of this experiment, envision the use of these peptides in a sequestered environment in the oral cavity for caries remineralization.

Finally, the relationship between breastfeeding and dental caries has been systematically and narratively reviewed with conflicting results between studies. In 2015 a new systematic review by Tham et al[296] reported that breastfeeding in infancy may protect against dental caries. Additional research is, however, needed to understand the increased risk of caries in children breastfed after 12 months.

Treatment strategies

The most common treatment by dentists for failed restorations after 10 years of placement has been to replace them. Although replacing a restoration is commonly preferred by most dentists, repairing it may be the more conservative treatment option. During a replacement, a significant amount of healthy tooth structure is disturbed when the preparation area is enlarged, and negative effects on tooth longevity have been observed. In addition, replacing a restoration has the drawbacks of being time-consuming, running the risk of converting it to a larger restoration, and the possibility of injuring the dentin-pulp complex. In contrast, repairing a failing restoration is a part of the minimally invasive dentistry philosophy, which seeks to ensure the preservation of healthy teeth, early detection of carious lesions, no or minimal surgical intervention, and keeping the teeth functional for life. The purpose of this double-blind clinical trial was to assess the longevity of repairs to localized clinical defects in composite resin restorations that were initially planned to be treated with a restoration replacement. The hypothesis was that repairing a restoration would recover its clinical condition and increase its longevity after the initial 10 years and would be similar to replacing the restoration. Fifty restorations, 25 for each group, were followed for 10 years and evaluated by blinded clinicians for marginal adaptation, secondary caries, anatomic form, and color. Over the 10 years, the performance of the repaired restorations was similar to that of the composite resins that were replaced, with the parameters of marginal adaptation, secondary caries, and anatomy behaving similarly in both groups. In spite of the many limitations of this study starting from the limited number of patients, the fact that the evaluators changed over the years, and not considering the type of restoration (class I or II), clinicians must consider this valuable clinical option when treating patients.[5]

Caries removal has been historically performed until only hard, dry dentin is found. Because this criterion has been considered subjective, more objective criteria like caries-detection dyes have been proposed. Both of these approaches focus on removing all infected dentin. Nevertheless, recent evidence suggests that such complete excavation might not be appropriate, especially in proximity to the pulp, whereas leaving bacteria under a restoration might be both inevitable and tolerable providing an adequate seal maintains the nutritional deprivation of the remaining microorganisms. Schwendicke et al[297] performed a systematic review on 26 articles to verify from clinical data the efficacy of incomplete caries removal on 1782 patients with 2555 teeth. Risk of complications, patient reported pain and need for anesthetic, the time required for excavation, and bacterial numbers, possible in only 5 studies, were evaluated for possible risk of bias and sensitivity analysis. In conclusion, not attempting to remove all softened or stainable dentin could reduce the risk of complications.

Chemomechanical removal appears equally effective and advantageous with regard to pain as reported by another systematic review on the subject[298] but is time consuming and of no advantage with regard to clinical outcomes. Data regarding other self-limiting cavity preparation methods were inadequate for definitive conclusions. The authors concluded that excavation criteria should be confirmed against clinically relevant results, not surrogates with limited significance.

A systematic review by Doméjean et al[9] examined the effectiveness of resin infiltration to arrest the progression of noncavitated caries lesions. Although to meet the strict selective criteria, only 4 articles were used for final analysis, the authors concluded that resin infiltration is a promising noninvasive approach and might be considered as an additional option to nonoperative and operative treatment approaches. Nevertheless, high-quality, long-term clinical trials are required to confirm the efficacy of resin infiltration for noncavitated caries lesions

in both deciduous and permanent teeth. In particular, in order to determine long-term benefits, comparisons need to be made between resin infiltration and remineralization strategies for enamel lesions and between RI and conventional restorations for dentinal lesions.

Finally, in an interesting systematic review, Schwendicke et al[299] studied the efficacy of cavity liners, a widespread preventive measure for dental caries among clinicians. Within the limitations of the review and the included studies, it was concluded that certain liners seem more able to achieve sterile cavities or reduce bacterial counts than others. In clinical practice, they added, "the performed excavation of carious dentin and the quality of the subsequently placed restoration might be more decisive than the decision for or against a specific liner."

Dental composite resins are the most widely used restorative materials in modern dentistry; however, among most of the restorative materials, composite resins have been shown to accumulate more biofilms and plaque in vivo. For this reason, attempts have been made to produce new composite resins containing antibacterial components without compromising the physical properties of material.[300] The main research fields are inclusion of antibacterial components in the resin material itself or a coating of highly hydrophilic bacteria repellent material on the surface. A Chinese-American study[301] of a new composite resin containing 2-methacryloyloxyethyl phosphorylcholine (MPC) and a quaternary ammonium dimethylaminohexadecyl methacrylate (DMAHDM) tried to combine both benefits in one material. The objects of the study were to develop a novel protein repellent and an antibacterial composite and to investigate the combined effects of MPC and DMAHDM on protein adsorption, dental plaque microcosm biofilm response, and mechanical properties of the composite. It was hypothesized that the composite resin containing MPC and DMAHDM would have good mechanical properties matching those with 0% MPC and 0% DMAHDM and those of a commercial control composite resin; that the composite resin containing MPC and DMAHDM would have much less protein adsorption than the controls; and that incorporating MPC or DMAHDM individually into composite resin would yield substantial decreases in biofilm growth on composite; and that incorporating both MPC and DMAHDM into composite resin would achieve much greater biofilm-inhibition than using MPC or DMAHDM alone.

An existing commercially available composite resin was modified for this study, and 9 specimens with different concentrations of antibacterial agents were tested. Only the concentration of 1.5% DMAHDM maintained the same physical properties of the unmodified composite resin and that was the concentration used for the study. Dental plaque microcosm biofilm formation and live/dead assay were performed (to test presence and vitality of biofilm), as well as MTT metabolic assay (a test for cellular vitality). Lactic acid production was also evaluated, and finally the bacterial colonies were counted (CFU standard technique).

The conclusion of the study was that the composite resin with 3% MPC showed a significant protein repellent ability and considerably reduced bacteria attachment. In addition, the use of dual agents, 3% MPC plus 1.5% DMAHDM, in the composite resin achieved the greatest reduction in biofilm growth and lactic acid production. The composite resin with 3% MPC plus 1.5% DMAHDM had physical properties that matched those of the commercially available composite resin without protein repellent and antibacterial properties. Although it was an in vitro study, it was well designed and executed by researchers with experience and many publications on dental caries. The novel composite resin with MPC plus DMAHDM is very promising in reducing biofilm formation and plaque buildup and inhibiting secondary caries, the main reason for failure of composite resin restorations. The method of dual agents MPC plus DMAHDM may have wide applicability to other bonding systems, composite resins, sealants, and cements.

Additional papers

An interesting paper from Japan,[302] although retrospective, studied the effect of secondhand smoking on teeth and whether there was an increased risk of caries. The only cohort study on this topic was a paper from Sweden investigating whether an increased risk of caries in 18 142 teenagers between 13 and 19 years of age could be linked to maternal smoking during early pregnancy and exposure to secondhand smoke and whether these associations may be confounded by unmeasured lifestyle factors such as tooth brushing.

Although no patients were seen for this study, the data were derived from the database of the Japanese Health System and are relevant because all women of childbearing age and children from pregnancy to 3 years of age residing in Kobe City participated in the health evaluation program. Children born between 2004 and 2010 in Kobe City (76 920) received municipal health evaluations at birth, 4, 9, and 18 months, and 3 years of age, and their records had information on household smoking status at 4 months of age and records of dental examinations at 18 months and 3 years of age. Qualified dentists assessed the oral conditions of the children at 18 months and 3 years of age through visual examination and not radiography. They divided each tooth into 1 of 7 types: normal, decayed, missing, filled, treated with silver diamine fluoride, observation required, or treated by a dental sealant. Teeth treated with silver diamine fluoride as well as decayed teeth were counted as decayed, and

this could be considered a limitation of the study because silver diamine fluoride can be used both as initial treatment for caries and for prevention. Thus, some teeth classified as carious may have not developed decay in the future.

The incidence of dental caries was defined as the occurrence of at least 1 decayed, missing, or filled tooth. The children were divided in 3 groups: no contact with smoke, with parents that smoked in the house but not in their presence, and with parents that smoked in their presence. A well-designed statistical analysis taking into consideration several possible confounding variables and adequate adjustments reported that children with family members who smoked had significantly more decayed, missing, or filled teeth than those with no smokers in the family. More specifically, exposure to tobacco smoke at 4 months of age was associated with an approximately twofold increase in the risk of caries, and the risk of caries also was 1.5-fold increased among those exposed to household smoking. The effect of maternal smoking during pregnancy was not statistically significant.

However, the same research group in a second similar research paper[303] in a different Japanese city demonstrated a positive correlation between maternal prenatal and perinatal smoking and increased dental caries in the deciduous teeth of their children. Although the retrospective design of the study may not establish direct causality, the high number of participants included and the well-designed statistical analysis suggest that the unhealthy role of secondhand smoking may be underestimated not only for the general health of children but also for the health of their teeth.

One of the greatest predisposing factors for dental caries is xerostomia. Prosthodontists are constantly challenged by patients who, for systemic or therapeutically induced reasons (drugs or radiation), lack adequate amounts of saliva. A clinical controlled research[304] of 40 patients with xerostomia secondary to radiation therapy for head and neck cancer suggested that the use of TENS, an inexpensive, easy to apply, and safe method, can significantly enhance salivary flow. Although the cohort was limited to radiated participants, these data could be extremely meaningful for the treatment of such a limiting condition, and further studies on a broader range of xerostomic patients are needed.

IMPLANT DENTISTRY

A total of 26 articles on implant dentistry have already been reviewed in this manuscript, primarily in the "Periodontics" and "Prosthodontics" sections, so this section will be somewhat abbreviated from previous years. One interesting study evaluated the effects of a change in a government-administered reimbursement system on prosthodontic treatment services received by patients covered by the program.[305] Prior to the policy change (July 1, 2008), patients over the 65 years of age received a higher subsidy for dental care than patients below the age of 65. After July 1, 2008, all patients received the same subsidy, which was at a lower rate than previously for the 65 and older group.

The study evaluated a database from the Swedish Social Insurance Agency for treatments provided between July 1, 2007 (before the change in reimbursement) to June, 30, 2009. Treatment rendered in the Public Dental Health Service and the private sector were analyzed. Data were retrieved for 722 842 adult patients covering a total of 1 339 915 reimbursed treatment items. After the change in the reimbursement system, there was a decrease in the proportion of items in patients 65 years of age and above. The authors concluded that irrespective of service provider, financial incentives such as reimbursement may influence the provision of prosthodontic treatment.

Another study examined mortality patterns in patients treated with implants to those of reference populations.[306] Patient cumulative survival rates (CSR) were calculated for 4231 patients treated with implants in a single clinic. Data for the reference population was obtained from the National Population Register in Sweden. Patients were arranged into age groups of 10 years, and the CSR of the implant patients compared with that of the reference population in relation to the age at surgery.

The study found that completely edentulous patients had a higher mortality rate than partially edentulous patients. Additionally, patients who received implants at a younger age had a similar or higher mortality than the reference population, and patients who received implants when they were older had lower mortality than comparable reference populations. The authors speculated that the differences in CSR were not related to implant treatment per se but reflected the variation in the general health of the compared groups.

A study evaluated the effects of fixed implant-supported prostheses (IFPD) versus implant-supported removable partial dentures (IRPD) on swallowing threshold, dietary intake, and oral HRQoL.[307] Twelve patients sequentially used both IRPD and IFPD prostheses. Swallowing threshold was assessed by counting masticatory cycles and determining median particle size. Nutritional intake was verified by a 3-day diet analysis. Oral HRQoL was measured with the Oral Health Impact Profile (OHIP-49).

Swallowing threshold was reduced in the IFPD group, and this group also had higher intake of fiber, calcium, and iron and lower consumption of cholesterol-rich food. The OHIP summary score and OHIP physical pain domain were lower in the IFPD group. The authors concluded that IFPD compared with IRPD leads to more

efficient mastication and improves dietary intake as well as oral HRQoL.

SUMMARY

It is clear that the dental profession is appropriately expending a great deal of time and money on research. The quality of research has been steadily improving over the past several years; however, there is lots of room for improvement. The large numbers of systematic reviews that fail to answer the basic research question because of studies that are poorly designed is evidence of this lack of quality. Still, many studies published in 2015 are important to help guide clinicians to the best treatment options. Hopefully, this review will assist dentists in identifying those studies.

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