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# What's new for the clinician – summaries of recently published papers (November 2025)

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## 1. EFFICACY OF DIFFERENT THERAPEUTIC OPTIONS FOR PAIN RELIEF AND TREATMENT OF BURNING MOUTH SYNDROME: A SYSTEMATIC REVIEW

Burning Mouth Syndrome (BMS) is a complex chronic pain condition characterised by a persistent burning sensation in the oral mucosa without clinically evident lesions. Its multifactorial and often idiopathic nature makes treatment challenging, necessitating a multifaceted approach. The efficacy of various therapeutic options is supported by evidence of varying quality, with no single universally effective treatment.

Systemic medications form a cornerstone of BMS management. **Clonazepam**, a benzodiazepine, has the strongest evidence for efficacy. The most supported regimen is the topical "swish-and-spit" method, which is believed to counteract central and peripheral neuropathic pathways by modulating oral sensory perceptions. Multiple randomised controlled trials (RCTs) have shown it to be significantly more effective than placebo in reducing pain. Systemic oral clonazepam is also used but carries a higher risk of sedation. *Alpha-lipoic acid (ALA)*, an antioxidant, has been extensively studied with mixed results. Early, smaller RCTs were promising, suggesting it could help repair nerve damage. However, more recent and larger systematic reviews and meta-analyses have concluded that ALA is not significantly more effective than placebo, casting doubt on its utility as a monotherapy.

**Antidepressants** are commonly employed, particularly low-dose **amitriptyline** or **selective serotonin reuptake inhibitors (SSRIs)**, but robust RCT evidence is lacking. Their use is primarily based on BMS's association with depression and anxiety and their known efficacy in other neuropathic pain conditions. **Gabapentin** and **pregabalin**, first-line treatments for neuropathic pain, are also used off-label for BMS, often showing benefit in refractory cases, though large-scale trials are needed.

**Cognitive Behavioural Therapy (CBT) and Psychological Interventions:** Given the strong link between BMS, anxiety, depression, and somatisation, psychological interventions are a critical component of treatment. Evidence from several studies demonstrates that CBT can be highly effective in reducing pain intensity and improving coping strategies and quality of life. It helps patients reframe their perception of pain and break the cycle of pain catastrophising. While not a direct pharmacological intervention, CBT is considered a first-line or adjunctive therapy by many specialists.

**Non-Pharmacological and Emerging Therapies: Non-invasive brain stimulation** techniques, particularly **transcranial magnetic stimulation (TMS)**, have shown promise in small trials. Repetitive TMS can modulate cortical excitability in brain regions involved in pain processing, providing significant relief for some patients. Similarly, *capsaicin* rinses (low-concentration) aim to desensitise oral nociceptors, though the evidence is preliminary and the initial burning sensation can limit tolerability.

In summary, the evidence supports a tiered, personalised approach to BMS management. Topical clonazepam is one of the best-evidenced first-line pharmacological treatments. Psychological interventions, particularly CBT, are equally vital and should be integrated early. For refractory cases, systemic neuropathic pain medications like gabapentin or off-label use of antidepressants may be necessary, despite a weaker direct evidence base. The mixed results for alpha-lipoic acid highlight the need for more rigorous, large-scale trials. Ultimately, managing patient expectations and combining pharmacological agents with psychological support appears to be the most effective strategy for this debilitating condition

Rossetti and colleagues (2025)[1] reported on a systematic review that sought to evaluate the efficacy of the different therapeutic options currently used to treat and relieve the pain of BMS, in order to provide better clinical guidance for the future.

### Methodology

This systematic review was conducted in accordance with PRISMA 2020 guidelines. A comprehensive literature search was conducted in February 2025, adhering to PRISMA guidelines, across three databases: PubMed, Google Scholar, and SciELO. The search strategy employed Medical Subject Headings (MeSH) and Boolean operators to maximise sensitivity and relevance.

In Google Scholar, a total of 4,680 records were retrieved. After the removal of duplicates, off-topic studies, studies outside the scope of the review, and those not classified as randomised controlled trials (RCTs), 4,494 articles were excluded. Additionally, four articles in German and 161 without full-text access were excluded. Notably, 21 of the selected articles from Google Scholar were also identified through PubMed. The SciELO search yielded six articles, all of which were excluded due to lack of full-text access. In PubMed, 905 records were identified. After screening, 881 articles were excluded for being duplicates, lacking full-text access, or not meeting the RCT criteria.

Following de-duplication and eligibility screening, a total of 24 full-text RCTs published since 2015 were selected for full-text review. After detailed assessment, three articles were excluded for either not addressing Burning Mouth Syndrome (BMS) or not meeting the inclusion criteria.

Thus, a final total of 21 full-text RCTs, published from 2015 onward, were included in this systematic review.

The search strategy was based on the PICO model (Population, Intervention, Comparison, Outcome), focusing on adult patients diagnosed with Burning Mouth Syndrome (BMS) undergoing therapeutic interventions for symptom relief. Eligibility was determined by predefined inclusion and exclusion criteria, emphasising methodological rigor and relevance to the research question. Data extraction, management, and evaluation were conducted using a systematic and standardised approach to ensure transparency and reproducibility.

A quantitative meta-analysis was deemed unfeasible due to substantial heterogeneity across multiple dimensions: (1) diversity of therapeutic interventions (topical vs. systemic vs. physical therapies); (2) variability in outcome measurement scales (VAS, NRS, categorical scales); (3) different treatment protocols and dosing regimens; (4) heterogeneous follow-up periods (2 weeks to 12 months); and (5) varying definitions of treatment success or "responder" criteria across studies.
The criteria for selecting studies ensured the inclusion of high-quality evidence relevant to the clinical question. Only randomised controlled trials (RCTs) or controlled clinical trials involving adult patients diagnosed with BMS were included. The primary outcome considered was the relief or reduction of oral burning sensation and associated symptoms such as xerostomia and dysgeusia.

For this review, "therapeutic intervention" was defined as any pharmacological (topical or systemic medications), non-pharmacological (physical therapies such as laser therapy, acupuncture), or complementary therapy specifically aimed at reducing oral burning sensation in BMS patients. Studies investigating multitherapy approaches (combination of two or more treatments) were included and analysed separately. Interventions had to be clearly described with sufficient detail regarding dosage, frequency, and duration to allow for replication.

Studies were excluded if they were observational, case reports, reviews, editorials, or involved patients with oral mucosal diseases other than BMS or paediatric populations. Language was restricted to English, Spanish and Portuguese to maintain accessibility for analysis. Studies were also excluded if interventions were: (1) purely diagnostic procedures without therapeutic intent; (2) general oral hygiene measures without specific BMS targeting; (3) interventions for conditions other than primary BMS; or (4) insufficiently described protocols preventing replication.

Trials were analysed independently and objectively, based on the predefined inclusion and exclusion criteria, to decide whether they should be included in the review. After this phase, the selected articles were carefully analysed. A third reviewer was consulted to help reach a final decision in cases of disagreement.

Full texts of all included studies were reviewed, and information was systematically organised in Microsoft Excel. According to the review protocol, key data extracted included: article details (title, year, authors, country), study objectives, patient population, methodology, and results.

Each study's design, purpose, and specific treatment—whether systemic, topical, pharmacological, non-pharmacological, or alternative—were carefully considered, along with the type of Burning Mouth Syndrome reported. Additional data included study participants' characteristics, use of placebo, treatment duration, follow-up periods, number of participants, sex, mean and median age, and diagnostic criteria for BMS.
Symptomatology, adverse effects, and comparisons between treatment strategies were also analysed in detail.
The included RCTs were independently evaluated using the JBI Critical Appraisal Checklist for Randomised Controlled Trials, assessing methodological quality and risk of bias across five domains: (1) Randomisation process; (2) Deviations from intended interventions; (3) Missing outcome data; (4) Outcome measurement; and (5) Selection of reported results.

### Results

Due to the heterogeneity in the included studies, no attempt was made to pool the data for a meta-analysis. Fourteen interventions were identified, including alpha-lipoic acid, topical/systemic clonazepam, low-level laser therapy (LLLT), capsaicin, melatonin, gabapentin, and cognitive-behavioural therapy. Topical clonazepam, alpha-lipoic acid, and LLLT consistently demonstrated the most significant symptom improvement with few mild adverse effects.

The overall quality assessment results showed that eleven studies were rated as low risk of bias, eight raised some concerns, and two were considered high risk.

### Conclusions

While topical clonazepam, alpha-lipoic acid, and low-level laser therapy (LLLT) emerged as potentially effective options in several RCTs, the overall strength of evidence is limited. These therapies appear promising, but further high-quality, larger randomised trials are needed before firm first-line recommendations can be made.

### Implications for practice

This study provides evidence-based guidance for clinicians in selecting effective treatments for BMS, emphasising tailored therapeutic approaches and the potential benefits of topical clonazepam, alpha-lipoic acid, and low-level laser therapy as first-line options.

### Reference

1. Rossetti, A., Teixeira, A. & Milhazes, N. Efficacy of different therapeutic options for pain relief and treatment of burning mouth syndrome: a systematic review. *Clin Oral Invest 29*, 551 (2025). https://0-doi-org.innopac.wits.ac.za/10.1007/s00784-025-06608-7

## 2. TREATMENT OF PERI-IMPLANTITIS WITH DIODE LASER OR MUCOSAL FLAP SURGERY: A CLINICAL RANDOMISED CONTROLLED TRIAL

Peri-implantitis affects 9–20 % of implants/implant patients and is currently treated mainly with open-flap surgery to debride and decontaminate the implant surface. Diode lasers (970 nm) can vaporise granulation tissue and kill sub-mucosal bacteria without raising bone temperature if used carefully. If this flapless approach produced healing similar to surgery it would offer a less-invasive first-line option with less morbidity. No previous RCT had tested a 970 nm diode laser used in this way for at least 6 months. This parallel-group equivalence trial therefore compared clinical, radiographic, patient-reported, immunological and microbiological outcomes 6 months after either single diode-laser de-epithelisation/decontamination or conventional mucosal-flap surgery in patients with established peri-implantitis.

## Methods

**Design:** Single-centre, examiner-unblinded, 6-month equivalence RCT (ClinicalTrials.gov NCT04249024, Stockholm regional ethics 2015/822-31/2).

**Population:** 33 consecutive referrals; 26 patients (29 implants) completed.

**Inclusion:** ≥ 18 y, ≥ 1 implant with PPD ≥ 6 mm + BOP/SOP and ≥ 2 mm radiographic bone loss after osseointegration. Exclusion: antibiotics, peri-implant therapy, MI, head-neck radiotherapy or i.v. bisphosphonates within 6 months.

**Randomisation:** Block randomisation (blocks 4/6) stratified by baseline mean PPD (< 4.5, 4.5–6.5, > 6.5 mm); pre-generated list; allocation after baseline examination.

**Interventions:**

- Laser group (14 patients/17 implants): flapless mechanical debridement (steel curette) if calculus present, then 970 nm diode laser, 1.2 W continuous-wave, 320 µm fibre, saline irrigation; fibre swept pocket-to-apical until entire defect irradiated (mean 314 s, 376 J).
- Surgery group (12 patients/12 implants): local anaesthesia, reversed-bevel incision, full-thickness mucoperiosteal flap, granulation tissue removal, titanium-brush implant surface cleaning, flap closure, 7–12-day suture removal. Both groups received identical oral-hygiene instruction and 0.2 % chlorhexidine rinses until first review.

Outcomes (baseline and 6 m; PROM also immediately and first-week):
Primary outcome measure: equivalence of mean change in PPD and marginal bone level (MBL, periapical radiographs, ImageJ).

Secondary outcome measure: full-mouth and site Plaque/BOP/Suppuration indices; patient VAS (0–100 mm) for pain, discomfort, satisfaction; stimulated saliva and peri-implant crevicular fluid (PICF) calprotectin, IL-1β, MMP-8; qPCR counts of Porphyromonas gingivalis, Tannerella forsythia, Treponema denticola, Fusobacterium nucleatum; post-study care needs.

Statistics: Per-protocol; equivalence zone ± 1 mm for PPD & MBL tested with two-one-sided tests (TOST, 90 % CI); other between-group comparisons by t, Mann–Whitney or $\chi^2$; $\alpha$ = 0.05.

## Results

Participants: Groups similar for age, sex, jaw distribution, implant brand; slightly more smokers and deeper baseline defects in surgery arm (non-significant).

**Primary outcomes:**

- PPD change laser –0.22 ± 0.91 mm vs surgery –0.90 ± 1.84 mm; 90 % CI lower bound –0.29 mm (p = 0.003) but upper bound +1.62 mm crossed +1 mm margin → equivalence rejected.
- MBL change laser –0.06 ± 1.02 mm vs surgery +0.32 ± 1.18 mm; 90 % CI lower –1.11 mm crossed –1 mm margin → equivalence rejected.
  Among the 17 patients whose PPD actually improved (9 surgery, 8 laser) surgery gave significantly greater reduction (–1.81 ± 0.94 mm vs –0.83 ± 0.40 mm, p = 0.016); MBL gains were similar in the smaller subgroup that improved.
- Hence for the **Primary outcomes:** Equivalence (±1 mm) was **not** shown for mean change in probing pocket depth (PPD) or marginal bone level (MBL).
  – PPD: laser –0.22 mm vs surgery –0.90 mm; 90 % CI crossed the equivalence margin.
  – MBL: minimal change in both groups; CI also crossed margin.
- **Clinical benefit:** In the ~60 % of patients whose PPD did improve, surgery gave **twice** the pocket reduction (–1.81 mm vs –0.83 mm, p = 0.016).
- **Patient experience:** Pain/discomfort scores low overall; surgery group had **higher pain and discomfort** during the first week (p ≤ 0.026).
- **Biology:** No meaningful inter-group differences in inflammatory biomarkers or major pathogens; slightly **higher P. gingivalis counts** persisted in the laser group.
- **Post-study care:** Laser patients needed **extra specialist revisits** more often (50 % vs 8 %, p = 0.05); equal numbers (4 per arm) already scheduled for re-treatment.

## Conclusions

A single 970 nm diode-laser session (1.2 W cw) produces **less pocket reduction** than conventional flap surgery and **cannot be claimed equivalent** at 6 months. Clinical "success" rates are similar, but surgery wins when measurable gain occurs. Laser treatment is **more comfortable initially** yet may require **more frequent re-care.**

## Implications for practice

- Do **not** substitute a single diode-laser decontamination for open-flap surgery when maximal pocket elimination or regenerative access is needed.
- Use the flapless laser as a **staged or palliative option** for high-risk, needle-phobic, or medically complex patients, **provided they accept closer monitoring and possible re-treatment.**
- **Counsel patients**: laser = less pain today, **possibly more visits tomorrow**; surgery = more pain this week, **deeper pocket reduction now**.
- **Larger, longer trials** required to clarify whether lesser early gains translate into higher long-term failure or implant loss.

## REFERENCE

1. Malmqvist S, Qadri T, Lira-Junior R, Boström EA, Gustafsson A, Belibasakis GN, Silbereisen A, Johannsen G, Johannsen A. Treatment of peri-implantitis with diode laser or mucosal flap surgery: A clinical randomized controlled trial. Journal of Periodontology. 2025 Mar 24.