de Souza RF, Lovato da Silva CH, Nasser M, Fedorowicz Z, Al-Muharraqi MA. Interventions for the management of temporomandibular joint osteoarthritis. Cochrane Database of Systematic Reviews 2012, Issue 4.

Glucosamine sulfate compared to ibuprofen for TMD osteoartritt

Patient or population: TMD osteoartritt
Intervention: Glucosamine sulfate
Comparison: Ibuprofen

Outcomes	**Anticipated absolute effects***(95% CI) **Risk with Glucosamine sulfat**	Relative effect (95% CI)	[1] of participants (Studies)	Quality of the evidence (GRADE)	Comments
Pain during function assessed with: VAS follow up: median 3 months	The mean pain during function in the intervention group was 0.73 RR higher (0.3 higher to 1.79 higher)	-	39 (1 RCT)	⊕⊕◯◯ LOW [1,2,3]	Significant improvement of pain during function both treatment groups. GS and ibuprofen reduce pain levels in patients with TMJ degenerative joint disease.
Reported pain-change from baseline assessed with: VAS follow up: 3 months	The mean reported pain-change from baseline in the intervention group was 4.57 lower (9.91 lower to 0.77 higher)	-	39 (RCTs)	⊕⊕◯◯ LOW [1,2]	Significant improvement of reported pain, change from baseline, both treatment groups. GS and ibuprofen reduce pain levels in patients with TMJ degenerative joint disease.
Pain free maximum jaw opening assessed with: mm follow up: 3 months	The mean pain free maximum jaw opening in the intervention group was 1.75 higher (4.1 lower to 7.6 higher)	-	39 (RCTs)	⊕⊕◯◯ LOW [1,2,3]	Significant improvement of pain free opening change from baseline, both treatment groups. GS and ibuprofen reduce pain levels in patients with TMJ degenerative joint disease.
BPI questionnaire, pain intensity, change from baseline assessed with: VAS follow up: 3 months	The mean BPI questionnaire, pain intensity, change from baseline in the intervention group was 2.69 lower (7.38 lower to 2 higher)	-	39 (RCTs)	⊕⊕◯◯ LOW [1,2]	Significant improvement of BPI- pain intensity, changes from baseline, both treatment groups. GS and ibuprofen reduce pain levels in patients with TMJ degenerative joint disease.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. One study, few participant
2. There is no placebo or other treatment group
3. Unclear sponsorship

Oppsummering: Resultatene viser at glucosaminsulfat og ibuprofen kan redusere smerter hos pasienter med TMD (osteoartritt/-artrose). Grunnlaget for dokumentasjonen er basert på fem RCT studier med lav kvalitet.

Mujakperuo HR, Watson M, Morrison R, Macfarlane TV. Pharmacological interventions for pain in patients with temporomandibular disorders. 2010 The Cochrane Collaboration.

Oral benzodiazepine compared to placebo for TMD treatment

Patient or population: TMD
Intervention: Oral benzodiazepine
Comparison: Placebo

Outcomes	Anticipated absolute effects*(95% CI)		Relative effect (95% CI)	[1] No of participants (Studies)	Quality of the evidence (GRADE)	Comments
	Risk with placebo	Risk with Oral benzodiazepine				
Jaw pain assessed with: VAS follow up: 3 weeks		The mean jaw pain in the intervention group was 20 MD lower (1.69 lower to 1.29 higher)	-	28 (1 RCT)	⊕⊕◯◯ LOW [1,2]	There was no statistically significant difference between the effect of clonazepam and placebo on jaw pain
Pain on palpation assessed with: VAS follow up: 2 months		The mean pain on palpation in the intervention group was 0 higher (0 higher to 0 higher)	-	20 (RCTs)	⊕⊕◯◯ LOW [1,3]	There was also no statistically significant difference between clonazepam and placebo in patient assessment of pain in the right temporomandibular joint.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Only one RCT with few participants
2. Allocation, free of other bias?
3. Adequate sequence generation, Allocation??

Oppsummering: Resultatene viser ingen forskjell på kjevesmerter for oralt administrerte benzodiapzepiner sammenlignet med placebo. Dokumentasjonen er vurdert å være av lav kvalitet. Grunnlaget for dokumentasjonen er basert på to studier med få deltakere og med risiko for bias.

Mujakperuo HR, Watson M, Morrison R, Macfarlane TV. Pharmacological interventions for pain in patients with temporomandibular disorders. 2010 The Cochrane Collaboration.

Gabapentin compared to placebo for TMD

Patient or population: TMD
Intervention: Gabapentin
Comparison: Placebo

Outcomes	**Anticipated absolute effects***(95% CI) **Risk with Gabapentin**	Relative effect (95% CI)	[1] of participants (Studies)	Quality of the evidence (GRADE)	Comments
Spontaneous pain assessed with: VAS follow up: 12 weeks	The mean spontaneous pain in the intervention group was 3.2 lower (4.71 lower to 1.69 lower)	-	50 (1 RCT)	⊕⊕◯◯ LOW [1,2]	In this study, gabapentin demonstrated a statistically significant effect over placebo in reducing spontaneous pain in the TMJ
Number of tender sites follow up: 12 weeks	The mean number of tender sites in the intervention group was 4.56 lower (6.99 lower to 2.13 higher)	-	50 (1 RCT)	⊕⊕◯◯ LOW [1,2]	In this study, gabapentin demonstrated a statistically significant effect over placebo in the number of tender sites on the muscles of mastication
Global function follow up: 12 weeks	The mean global function in the intervention group was 1.5 lower (3.1 lower to 0.1 higher)	-	50 (1 RCT)	⊕⊕◯◯ LOW [1,2]	Assessment of global function showed no significant difference between the gabapentin and placebo groups

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Only one study, few participants
2. pharmaceutical industry sponsorship

Oppsummering: Resultatene viser redusert smerte og redusert antall ømme punkter hos TMD-pasienter ved bruk av gabapentin sammenlignet med placebo. For generell funksjon var det ingen statistisk signifikant forskjell mellom gabapentin og placebo. Grunnlaget for dokumentasjonen er basert på en studie med lav kvalitet.

Oppsummering: Trisykliskeantidepressiva (TCA) i behandling av TMD

GRADE kunne ikke benyttes, fordi ingen av studiene tilfredsstilte de metodiske og statistiske kravene for denne typen kvalitetsvurdering.

Litteratur: Cascos-Romero J, Vázquez-Delgado E, Vázquez-Rodríguez E et al. The use of tricyclic antidepressants in the treatment of temporomandibular joint disorders: Systematic review of the literature of the last 20 years. Med Oral Patol Oral CirBucal 2009;14:E3-7

Cascos-Romero et al. (2009) brukte en graderingsmetode (tilsvarende GRADE) anbefalt av The National Health and Medical Research Council (NHMRC) og konkluderte:
According to the principals of evidence-based dentistry, there is currently a scientific evidence level B in favor of using TCAs for the treatment of TMDs.
No studies on this topic exist that fulfill the conditions for classification as scientific evidence level 1 according to SORT criteria. This means that the results published in the literature should be analyzed with caution since none have sufficient scientific basis, either because the sample size is inadequate, methodological defects are present, for example the lack of homogeneity of the populations studied, or, as commented above, because the results are extrapolated.
There are no scientifically sound studies that demonstrate the effectiveness of TCAs in the treatment of TMDs, therefore, more controlled clinical trials are necessary to demonstrate this hypothetical efficacy, and to assess the dose required for each pathology type and its associated side effects, among other parameters.

Tolkning

- Level A: Good scientific evidence suggests that the benefits of the clinical service substantially outweigh the potential risks. Clinicians should discuss the service with eligible patients.
- **Level B: At least fair scientific evidence suggests that the benefits of the clinical service outweigh the potential risks. Clinicians should discuss the service with eligible patients.**
- Level C: At least fair scientific evidence suggests that there are benefits provided by the clinical service, but the balance between benefits and risks are too close for making general recommendations. Clinicians need not offer it unless there are individual considerations.
- Level D: At least fair scientific evidence suggests that the risks of the clinical service outweigh potential benefits. Clinicians should not routinely offer the service to asymptomatic patients.
- Level I: Scientific evidence is lacking, of poor quality, or conflicting, such that the risk versus benefit balance cannot be assessed. Clinicians should help patients understand the uncertainty surrounding the clinical service.

Vidor LP, Torres ILS, De Souza ICC, Fregni F, Caumo W. Analgesic and sedative effects of melatonin in temporomandibular disorders: A double-blind, randomized, parallel-group, placebo-controlled study. Journal of Pain and Symptom Management 2013;46(3):422-32.

Summary of findings:

Melatonin compared to placebo for TMD

Patient or population: TMD
Intervention: Melatonin
Comparison: Placebo

Outcomes	**Anticipated absolute effects***(95% CI) **Risk with Melatonin**	Relative effect (95% CI)	[1] of participants (Studies)	Quality of the evidence (GRADE)	Comments
Pain reduction assessed with: VAS, PPT follow up: 28 days	The mean pain reduction in the intervention group was 44 adjusted MD lower (57 lower to 26 lower)	-	26 (RCTs)	⊕◯◯◯ VERY LOW [1 2 3]	Significant reduced pain scores, increased pressure pain threshold compared with placebo.
Decreasing of analgesic doses follow up: 28 days	The mean decreasing of analgesic doses in the intervention group was 0.6 adjusted MD lower (0.94 lower to 0.41 lower)	-	26 (RCTs)	⊕◯◯◯ VERY LOW [1 2 3]	Significant decreased analgesic doses compared to placebo.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Only one study
2. Few participants
3. Kort oppfølgningsperiode

Oppsummering: Resultatene viser redusert smerte og redusert bruk av smertestillende medikamenter hos TMD-pasienter ved bruk av melatonin sammenlignet med placebo. Grunnlaget for dokumentasjonen er basert på en studie med få deltakere, og på studier som er beheftet med stor risiko for systematiske skjevheter/feil i effektestimatene. Dokumentasjonen er vurdert å være av veldig lav kvalitet.