

Bucharest 2-4 October
2025

8th
International
Symposium
Intra
Articular
Treatment



IA use of NSAIDs: where we are

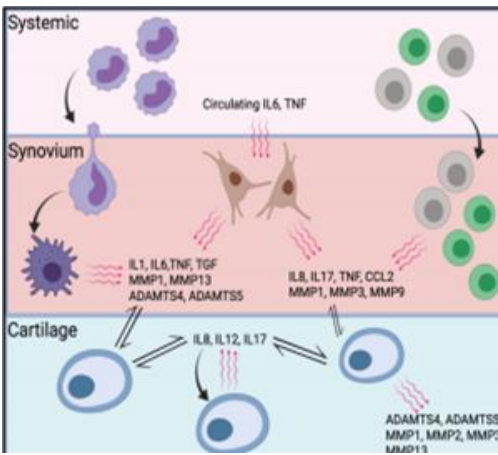
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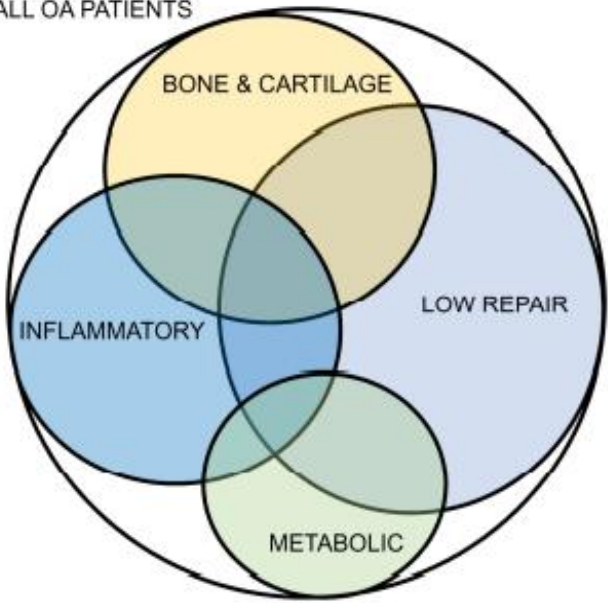
2. Unit of Rheumatology, Ospedale S. Pietro FBF, Rome, Italy

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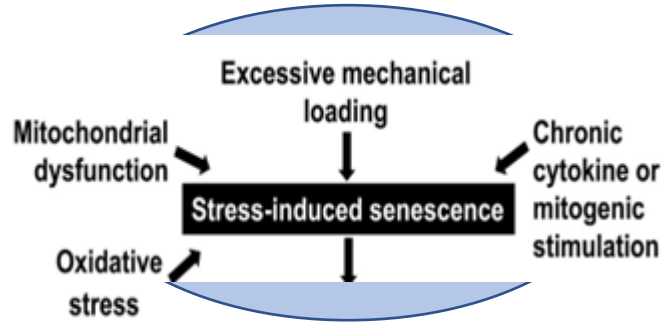
Author has nothing to
disclose



ALL OA PATIENTS

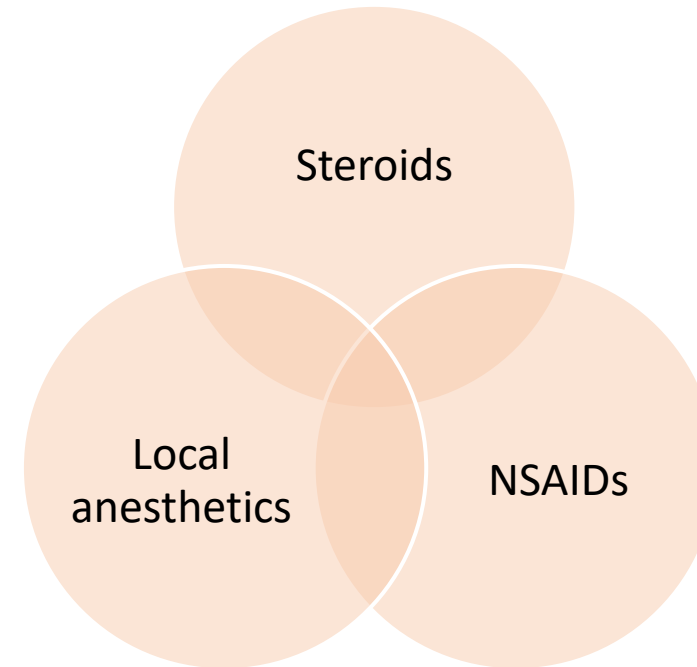
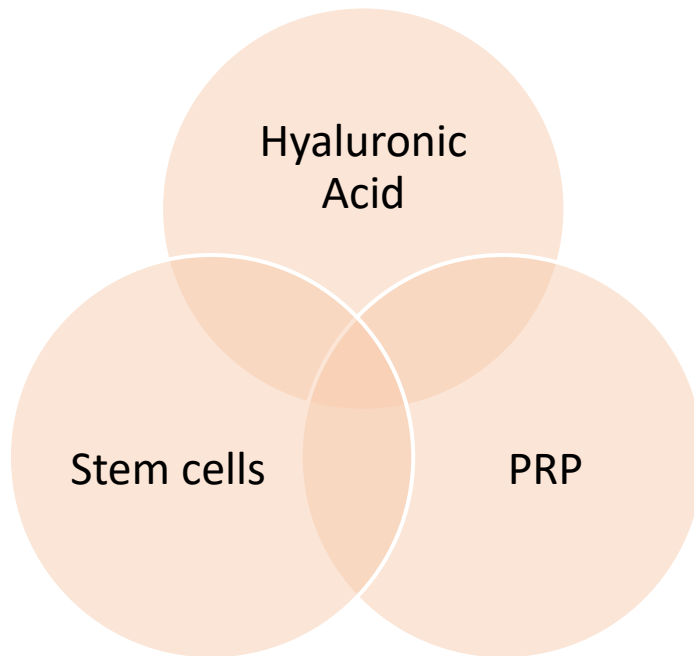


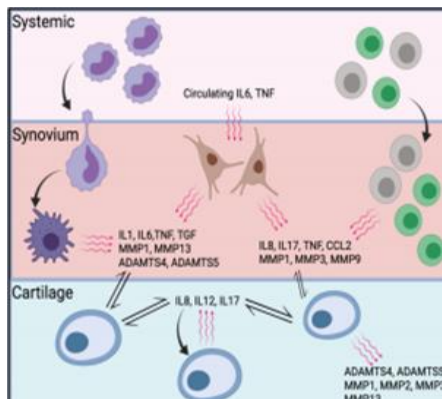
Adiponectin	Adipocyte
Leptin	Adipocyte, Chondrocyte
Resistin	Adipocyte, osteoblast, osteoclast, chondrocyte, macrophage
Chemerin	Adipocyte, immune cell



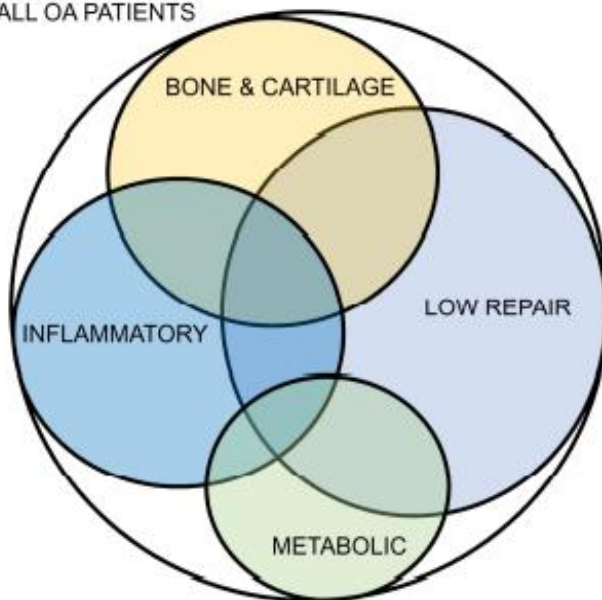
INJECTION THERAPY

The most commonly used products for intra-articular injections are:





ALL OA PATIENTS



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i. a. CS

i. a. NSAIDs?

NSAIDs in injection therapy

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NSAIDs are anti-inflammatory drugs widely used in the treatment of musculoskeletal disorders. NSAIDs' mechanism of action is based on the inhibition of factors involved in the inflammatory cascade process, in particular the **cyclooxygenase enzymes *COX-1 and COX-2***.

NSAIDs' actions



Anti-inflammatory

Analgesic

The **most common administration route is oral**, followed by **intramuscular**, **Mesotherapy** and **intravenous** administration.

Intra-articular administration, on the other hand, has been **less successful** and is currently the least used.

MATERIALS AND METHODS

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Currently, the **number of studies** evaluating the **efficacy of NSAIDs in injection** therapy and directly comparing their effects with other injectable therapies is **still limited**.

Our work focused on the **review** of such works in the scientific literature via *PubMed*.



SEARCH STRING:

(Injections OR intra- articular injection) and (NSAID OR Anti- Inflammatory Agents, Non- Steroidal OR Coxib OR Cyclooxygenase Inhibitors OR Cyclooxygenase 2 Inhibitors)

FILTERS: *5 years, humans*

MATERIALS AND METHOD

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Intra-articular injection therapy with NSAIDs: review of literature on major applications and clinical efficacy in musculoskeletal disorders.
Study Flow Chart

Identification

Records identified from PubMed (n = 1011)



Records removed *before screening* :
Not in English (n= 49)



MATERIALS AND METHODS

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Screening

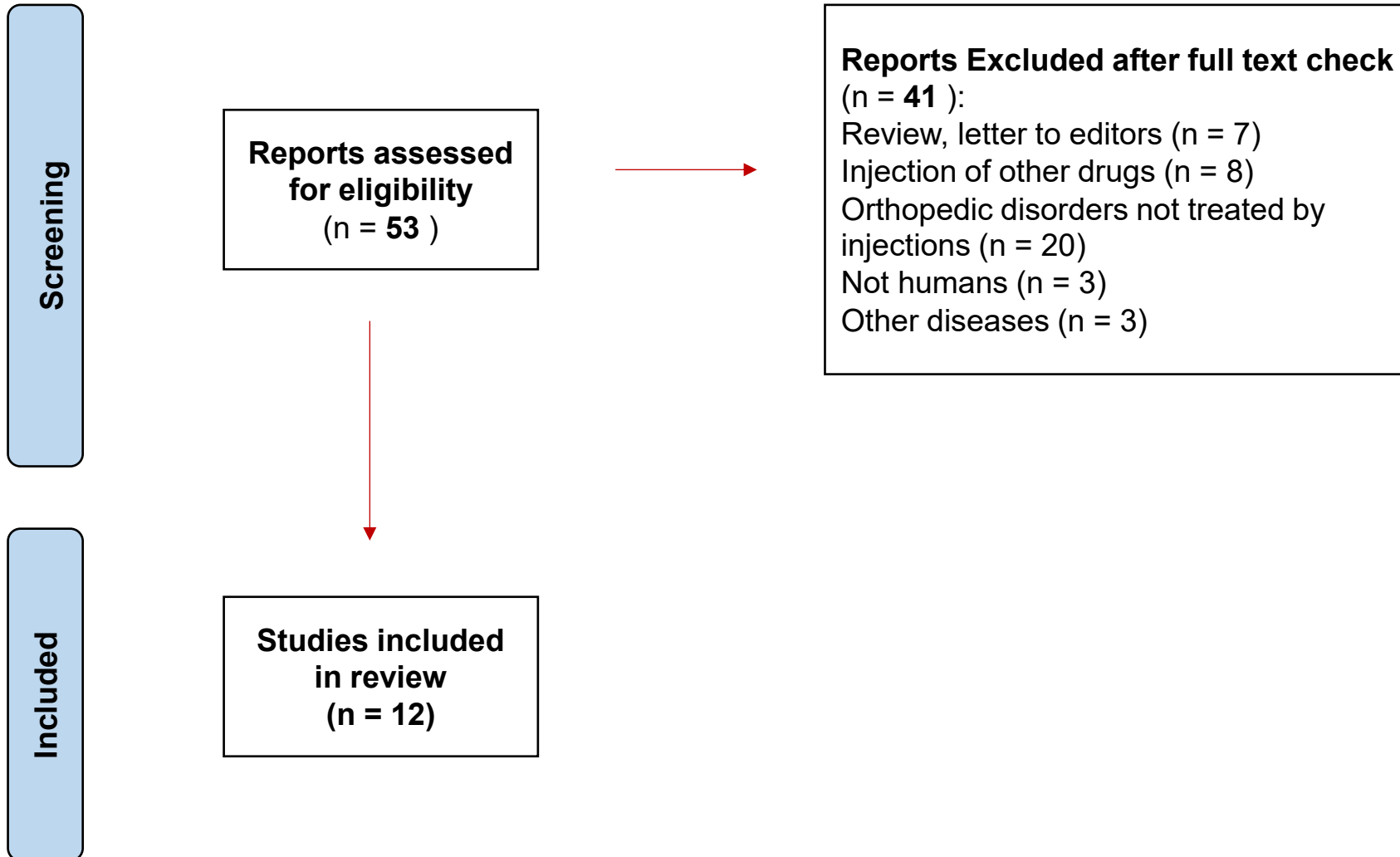
Records screened
(n = 962)

Records Excluded (n = 909):

Review/letter to the editor/Comment/trial proposal (n = 103)
Not Humans (n = 29)
Injection of other drugs (n = 60)
Orthopedic disorders not treated by injections (n = 112)
Arthritis not treated by injections (n = 44)
Non-musculoskeletal disorders
Nervous system (n = 53)
Genitourinary system (n = 45)
Gastrointestinal system (n = 27)
Visual system (n = 49)
Endocrine system (n = 9)
Respiratory system (n = 11)
Cardiovascular system (n = 43)
Autoimmune disorders (n = 11)
Dental disorders (n = 11)
Neonatal and pediatric diseases (n = 9)
Oncological diseases (n = 84)
Sars-CoV2 (n = 12)
Chinese Traditional Medicine (n = 11)
Dermatologic conditions (n = 32)
Pharmacology and drug trials (n = 145)
Surgery (n = 9)

MATERIALS AND METHODS

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OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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- ❖ Kubo et al performed a randomised double-blind study on **Diclofenac- hyaluronate compared to placebo** in **hip, ankle, shoulder** and **elbow osteoarthritis**
- ❖ Koh et al **compared** the efficacy of intra-articular injections of **hyaluronic acid associated with ketorolac**, with that of **HA alone**, for osteoarthritis of the **carpometacarpal joint of the thumb**

Kubo T, Kumai T, Ikegami H, Kano K, Nishii M, Seo T. Diclofenac- hyaluronate conjugate (diclofenac et al hyaluronate) intra -articular injection for hip, ankle , shoulder , and elbow osteoarthritis : a randomized controlled trial. BMC Musculoskeletal Disord . 2022 Apr 20;23(1):371. doi :10.1186/s12891-022-05328-3.

Koh SH, Lee SC, Lee WY, Kim J, Park Y. Ultrasound-guided intra- articular injection of hyaluronic acid and ketorolac for osteoarthritis of the carpometacarpal joint of the thumb : A retrospective comparative study. Medicine (Baltimore). 2019 May;98(19):e15506. doi : 10.1097/MD.00000000000015506.

OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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- ❖ Nishida et al conducted randomized, double-blind, placebo-controlled phase II and phase III studies on the **efficacy and safety** of intra-articular injection of **Diclofenac associated with Hyaluronic Acid** in the conservative treatment of knee osteoarthritis

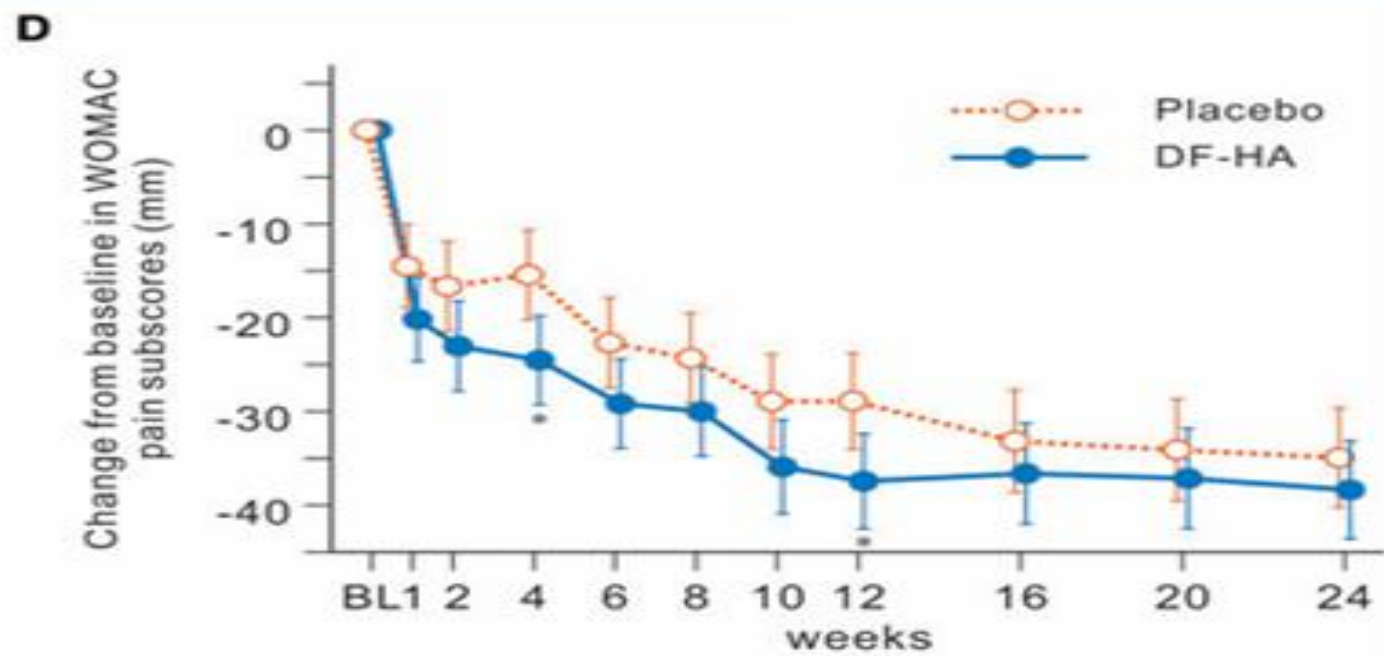


The same group subsequently recorded the results obtained with the combined Diclofenac + Hyaluronic Acid injection therapy in a **follow-up study after 1 year** in people who had received a total of 13 injections in the main joints: **knee, hip, ankle, shoulder and elbow**

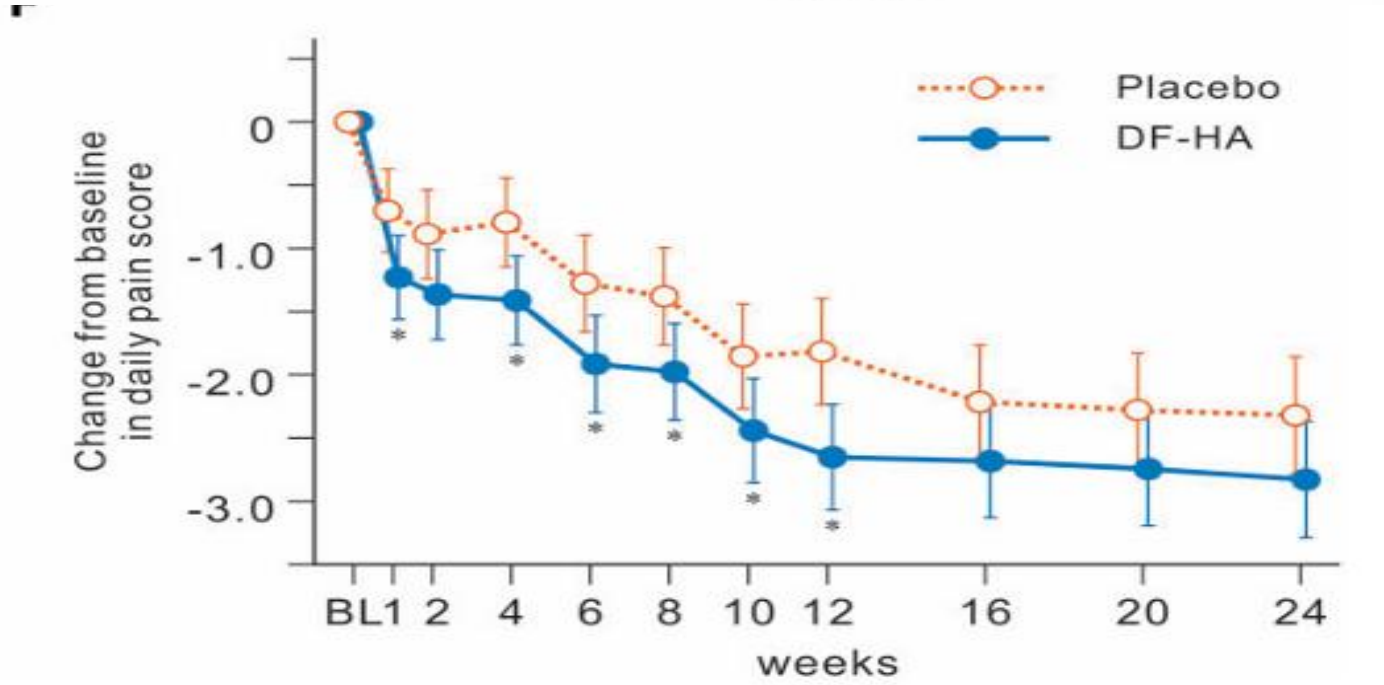
Nishida Y, Kano K, Nobuoka Y, Seo T. Efficacy and Safety of Diclofenac -Hyaluronate Conjugate (Diclofenac Etalhyaluronate) for Knee Osteoarthritis : A Randomized Phase III Trial in Japan. Arthritis Rheumatol . 2021 Sep;73(9):1646-1655. doi : 10.1002/art.41725. Epub 2021 Jul 27.

Nishida Y, Kano K, Nobuoka Y, Seo T. Sustained -release diclofenac conjugated to hyaluronate (diclofenac etalhyaluronate) for knee osteoarthritis : a randomized phase 2 study. Rheumatology (Oxford). 2021 Mar 2;60(3):1435-1444. doi : 10.1093/ rheumatology /keaa605. PMID: 33006602;

Nishida Y, Kano K, Osato T, Seo T. Open-label phase 3 study of diclofenac conjugated to hyaluronate (diclofenac etalhyaluronate : ONO-5704/SI-613) for treatment of osteoarthritis : 1-year follow-up. BMC Musculoskeletal Disord . 2021 Mar 1;22(1):233. doi :10.1186/s12891-021-04108-9.



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OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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❖ Akhtar et al **compared** intra-articular injections with **Ketorolac** and **Hyaluronic Acid** on pain control in **adhesive capsulitis of the shoulder**

➡ injections associated with lidocaine and epinephrine

❖ Jurgensmeier et al evaluated the **non-inferiority** of intra-articular injections of **Ketorolac** compared to **Triamcinolone** in the treatment of **hip and knee osteoarthritis**

➡ in this case both drugs were associated with the administration of ropivacaine

Akhtar M, Nadeem RDA, Shah Gillani SF, Cheema OI, Nadeem MR. Comparison of intra articular NSAID (ketorolac) injection versus hyaluronic acid injection for the mean decrease of pain score (according to UCLA shoulder rating scale) in the management of adhesive capsulitis . Pak J Pharm Sci. 2019 May;32(3):953-956.

Jurgensmeier K, Jurgensmeier D, Kunz DE, Fuerst PG, Warth LC, Daines SB. Intra- articular Injections of the Hip and Knee With Triamcinolone vs Ketorolac : A Randomized Controlled Trial. J Arthroplasty . 2021 Feb;36(2):416-422. doi :10.1016/j.arth.2020.08.036. Epub 2020 Aug 22.

OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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Yilmaz et al performed **comparing three groups** of patients **randomized** and treated, respectively, with intra-articular injection of the **knee**:

1. **Tenoxicam**
2. **Corticosteroids**
3. **Tenoxicam + Corticosteroids**

This study aimed to evaluate the **efficacy of the drug combination compared to single therapy** over a prolonged period of **up to 6 months from the first injection**



The evaluation of the effectiveness of intra-articular steroid, tenoxicam, and combined steroid–tenoxicam injections in the treatment of patients with knee osteoarthritis

Ebru Yilmaz¹

Variables	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)	p
Age (year)	68.07 ± 8.08	65.83 ± 10.13	67.07 ± 6.01	N.S.
Sex				
Female	19 (63.3%)	22 (73.3%)	15 (50.0%)	N.S.
Male	11 (36.7%)	8 (26.7%)	15 (50.0%)	
Duration of symptoms (months)	51.03 ± 49.29	57.67 ± 61.69	50.80 ± 40.68	N.S.
Occupation				
Housewife	19 (63.3%)	21 (70.0%)	15 (50.0%)	N.S.
Farmer	7 (23.3%)	4 (13.3%)	5 (16.7%)	
Worker	1 (3.3%)	1 (3.3%)	5 (16.7%)	
Cook	1 (3.3%)	2 (6.7%)	0 (0.0%)	
Officer	1 (3.3%)	2 (6.7%)	4 (13.3%)	
Driver	1 (3.3%)	0 (0.0%)	1 (3.3%)	
Body mass index (BMI)	29.50 ± 5.56	29.06 ± 4.05	32.40 ± 5.79	N.S.
Affected side				
Right	3 (10.0%)	5 (16.7%)	3 (10.0%)	N.S.
Left	4 (13.3%)	1 (3.3%)	2 (6.7%)	
Bilateral	23 (76.7%)	24 (80.0%)	25 (83.3%)	
Kellgren–Lawrence scale				
Stage 1	17 (56.7%)	16 (53.3%)	17 (56.7%)	N.S.
Stage 2	13 (43.3%)	14 (46.7%)	13 (43.3%)	

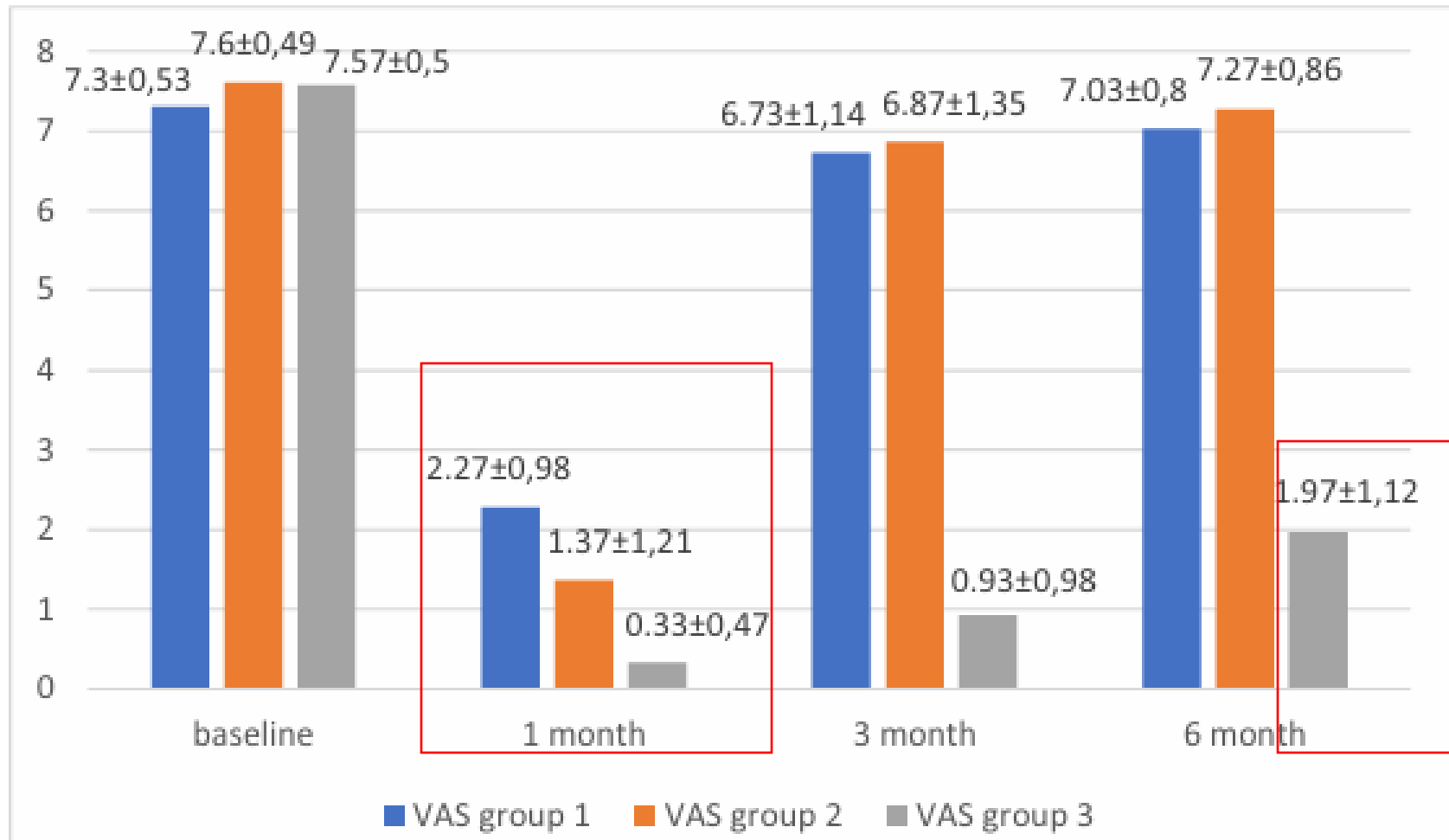
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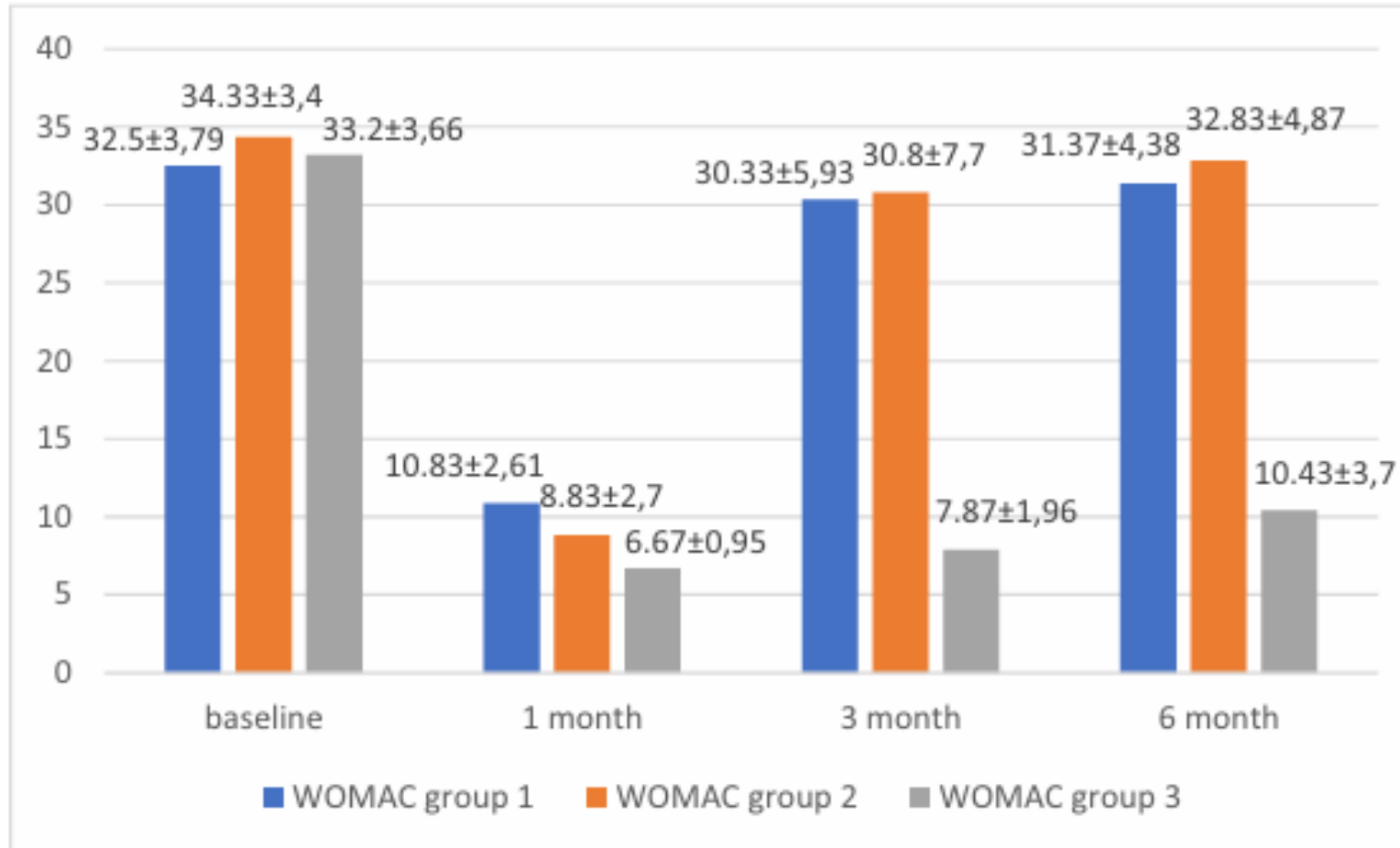


The evaluation of the effectiveness of intra-articular steroid, tenoxicam, and combined steroid-tenoxicam injections in the treatment of patients with knee osteoarthritis

Ebru Yilmaz¹

Bucharest 2-4 October 2025





OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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❖ Yapici-Yavuz et al. compared intra-articular injection therapy with:

- a. **Methylprednisolone acetate**
 - b. Sodium hyaluronate
 - c. **Tenoxicam**
- } after arthrocentesis

in the treatment of non-reducible disc displacement in the
temporomandibular joint

Yapici-Yavuz G, Şimşek -Kaya G, Oğul H. A comparison of the effects of Methylprednisolone Acetate, Sodium Hyaluronate and Tenoxicam in the treatment of non- reducing disc displacement of the temporomandibular joint. Med Oral Patol Oral Cir Bucal . 2018 May 1;23(3):e351-e358. doi :10.4317/medoral.22237.

OBJECTIVES OF THE STUDIES INCLUDED IN THE REVIEW

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❖ 2 studies evaluated intra-articular injections of NSAIDs **after surgery**,
focused mainly on pain:

- 1) Khan et al compared **Ketorolac** with **placebo**, after outpatient **knee surgery** such as meniscectomy, diagnostic synovial biopsies, and removal of worn cartilage.
- 2) Sicard et al compared local injections of **ketoprofen associated with ropivacaine** with interscalene nerve block in the management of early postoperative pain **after shoulder arthroplasty**

Khan Niazi AS, Bajwa MA, Zahra M, Khan Niazi MU, Zainab I, Anwer A. Efficacy Of Intra- Articular Ketorolac And Lignocaine On Post-Operative Pain Relief After Arthroscopic Knee Surgery. J Ayub Med Coll Abbottabad . 2022 Apr-Jun;34(2):273-278. doi :10.55519/JAMC-02-8647.

Sicard J, Klouche S, Conso C, Billot N, Auregan JC, Poulain S, Lespagnol F, Solignac N, Bauer T, Ferrand M, Hardy P. Local infiltration analgesia versus interscalene nerve block for postoperative pain control after shoulder arthroplasty : a prospective , randomized , comparative noninferiority study involving 99 patients . J Shoulder Elbow Surg . 2019 Feb;28(2):212-219. doi : 10.1016/j.jse.2018.09.026. Epub 2018 Dec 10.

RESULTS & DISCUSSION

- ✓ The results obtained show that injection therapy with NSAIDs determines a **functional improvement** and an **analgesic effect non-inferior to corticosteroid** treatment in **hip and knee osteoarthritis** (*Jurgensmeier et al*).
- ✓ The **association of an NSAID with a corticosteroid seems to give a more effective result**, compared to the single therapies, both in terms of **functional improvement and pain reduction** in cases of grade 1 or 2 knee osteoarthritis (*Yilmaz et al*)

RESULTS & DISCUSSION

- ✓ The combination between **NSAIDs** and **hyaluronic acid** appeared **effective, fast-acting and long-lasting** in the conservative therapy of knee osteoarthritis (*Nishida et al*)



- ✓ Interestingly, in an **initial evaluation phase**, the injection of the **two combined products** appears to determine **more significant improvements** in the **hip and knee** joints than in the shoulder and elbow.

RESULTS & DISCUSSION

- ✓ **NSAID + hyaluronic acid injection** had a **more rapid analgesic effect** than **single therapy** with the administration of **HA alone** on **carpometacarpal joint** osteoarthritis (*Koh et al*)
- ✓ The direct **comparison** of the use of **NSAID** and **HA** injections on **adhesive capsulitis of the shoulder** showed **equivalent efficacy** of the two treatments **on pain** improvement, but **NSAIDs appeared to have a more rapid effect** (*Akhtar et al*)

RESULTS & DISCUSSION

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- ✓ Injection therapy with NSAIDs has also appeared **effective in controlling postoperative pain after arthroscopic knee surgery**, with a better outcome than the use of the anesthetic drug alone (*Khan Niazi et al*)
- ✓ **Promising results** emerged also on **NSAIDs injections compared to Methylprednisolone acetate** in the temporomandibular joint (*Yapici-Yavuz et al*)

CONCLUSIONS

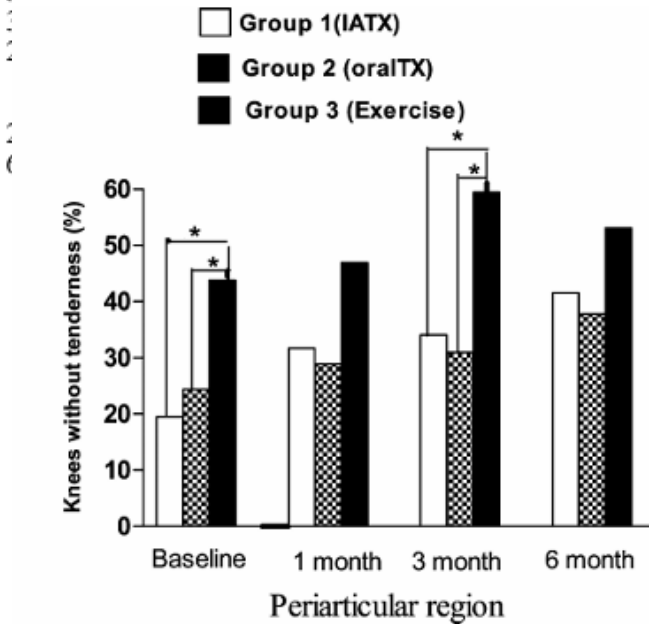
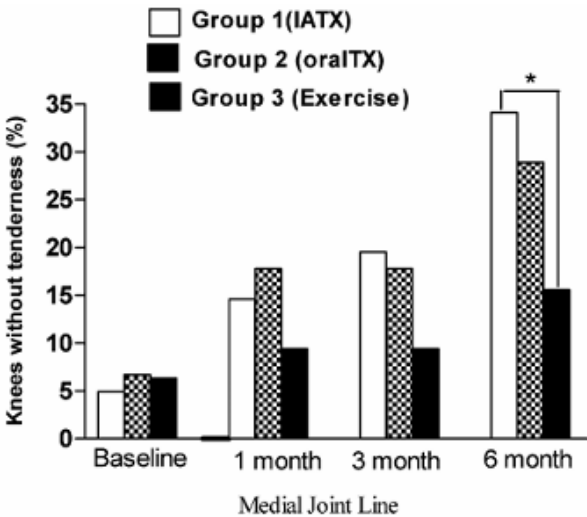
Randomized Controlled Trial > Clin Rheumatol. 2006 Feb;25(1):54-61.

doi: 10.1007/s10067-005-1136-3. Epub 2005 Oct 15.

Comparison of intra-articular tenoxicam and oral tenoxicam for pain and physical functioning in osteoarthritis of the knee

Zeliha Unlu ¹, Kamuran Ay, Cigdem Tuzun

	Group 1, IATX (n = 23)	Group 2, Oral TX (n = 26)	Group 3, exercise (n = 20)
Mean age (years)	57.1 ± 10.2 (38–77)	54.8 ± 9.1 (40–76)	52.2 ± 7.9 (38–68)
Body mass index (kg/m ²)	30.7 ± 5.5 (21–47)		



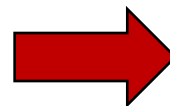
“...There was no significant difference between the oral and intra-articular tenoxicam treatment regimens. The results of this study showed that treatment of OA of the knee with intra-articular tenoxicam is as effective as that with oral tenoxicam. It can be thought that intra-articular administration can be preferred to oral therapy due to minimal possibility of systemic side effects...”

CONCLUSIONS

- ✓ **Intra-articular injection therapy with NSAIDs appears as a potential alternative** for achieving **rapid-onset analgesic relief** in both primary osteoarthritis and pain management after major joint surgery.
- ✓ **NSAIDs could be associated with HA** to potentially **reduce chondrotoxicity** and **improve joint rheology and function**
- ✓ NSAIDs injection therapy may **reduce systemic side effects** of oral treatment
- ✓ NSAIDs injection therapy emerged as **non-inferior to corticosteroid** treatment in **hip and knee osteoarthritis** (*Jurgensmeier et al*)

Could IA NSAIDs therapy?

- **Inflammatory phenotype**
- **Not eligible to IA steroids**



**Same
efficacy**



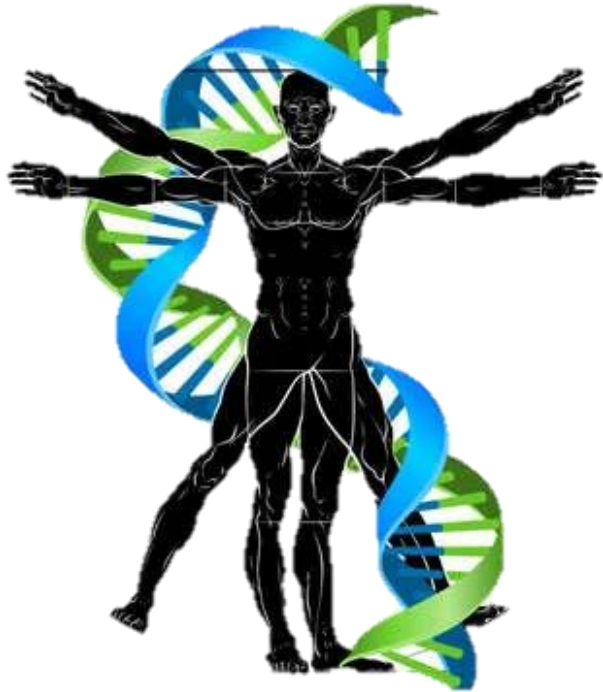
**Better
Safety**

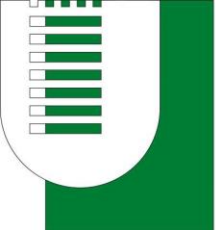
CONCLUSIONS

Future studies appear necessary to verify the efficacy and safety of intra-articular injection therapy with NSAIDs, also on larger population samples.

Greater standardization in research methods would allow for a higher level of evidence in the results.

The ultimate goal should remain the evaluation of the potential use of this treatment within the **Individual Rehabilitation Project**, aimed at functional recovery and improving the **QUALITY OF LIFE**

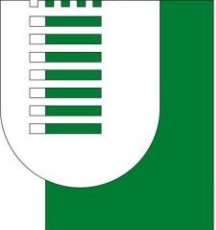




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Thank you for your attention!



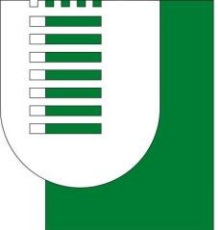
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IA use of NSAIDs: where we are

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