

EDITORIAL UVODNIK

FROM TREATMENT GUIDELINES AND CONSENSUS STATEMENTS TO REAL-WORLD IMPLEMENTATION – TRANSFORMING OSTEOARTHRITIS CARE THROUGH PHENOTYPIC STRATIFICATION AND MULTIDISCIPLINARY MANAGEMENT

OD SMERNICA ZA LEČENJE I IZJAVA O KONSENZUSU DO PRIMENE U STVARNOM SVETU – TRANSFORMISANJE LEČENJA OSTEOARTRITISA FENOTIPSKOM STRATIFIKACIJOM I MULTIDISCIPLINARNIM PRISTUPOM

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Introduction

Osteoarthritis (OA) is the most prevalent and disabling form of arthritis worldwide [1–3]. The current OA management landscape is characterized by a significant discordance between guideline recommendations and their implementation in primary care. Although numerous clinical practice guidelines exist [4–6], they often contain subtle inconsistencies and, more importantly, fail to adequately account for the substantial heterogeneity and multimorbidity that characterize the OA population [7]. Phenotypic heterogeneity in OA [8,9] manifests across multiple domains, including structural, inflammatory, metabolic, and pain-related pathways. This diversity is primary key reason why single-agent or unimodal treatments frequently fail to provide satisfactory outcomes, contributing to patient dissatisfaction and placing and increasing and unsustainable burden on primary healthcare systems [10]. To address these challenges, the OA research and clinical development communities must shift toward therapeutic strategies that are both multimodal in application and stratified in design, while also prioritizing research equity with

respect to sex [11,12], race, and geographical diversity [13].

The Inadequacies of Unimodal Care

The complexity of OA-related pain, particularly in moderate to severe knee OA, underscores the limitations of traditional single-intervention approaches [4,5,14]. It is now well established that the pathophysiology of OA extends far beyond the outdated concept of “osteoarthrosis”, which implied simple mechanical wear and tear [15]. Instead, OA represents a multifactorial disease involving a complex interplay between low-grade synovial inflammation, subchondral bone remodelling [16,17], meniscal degeneration, and both peripheral and central sensitization of the nervous system [18]. Consequently, reliance on a single therapeutic modality – whether pharmacological, such as oral non-steroidal anti-inflammatory drugs (NSAIDs), or non-pharmacological, such as physical therapy – is often insufficient to address the full spectrum of symptoms or to meaningfully improve quality of life in patients with OA. Major clinical guidelines, including those published by the European

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Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) and the Osteoarthritis Research Society International (OARSI), broadly converge on core management principles, including patient education, structured exercise, and weight management [4,19]. However, discrepancies remain even within these consensus recommendations [4,20]. Such variation reflects the evolving nature of the evidence base and highlights the need for clinicians to translate complex and sometimes inconsistent guidance into coherent, patient-specific treatment strategies. Addressing these challenges requires a multidisciplinary management approach that integrates pharmacological therapy, physical rehabilitation, and psychological support – such as cognitive behavioural strategies – tailored to the individual patient's pain profile, functional deficits, and overall health status.

Stratification and the Promise of Personalized Medicine

The ultimate objective in OA management is the implementation of truly stratified care, in which treatment strategies are tailored to the patient's underlying disease phenotype [21,22]. Moving beyond the traditional generic diagnosis of knee OA requires identifying the dominant drivers of disease in individual patients – whether inflammatory, metabolic, or mechanical [9,23,24]. Achieving this precision medicine approach in OA will require the integration of emerging biomarkers and advanced imaging techniques to classify patients into clinically meaningful subgroups [22]. For example, patients presenting with high levels of synovial inflammation detected through ultrasound or magnetic resonance imaging (MRI) may benefit most from targeted anti-inflammatory therapies or intra-articular interventions before other treatments are considered [25].

Conversely, patients with predominantly mechanical symptoms and minimal inflammatory activity may respond better to biomechanical interventions such as orthotic devices, targeted rehabilitation, or, in selected cases, surgical correction of malalignment. This paradigm shift necessitates clinical assessment tools that extend beyond basic pain scales and subjective questionnaires in order to capture the relative contributions of different disease mechanisms.

The development of simple yet robust digital tools capable of facilitating early phenotyping – poten-

tially through gait analysis or body composition assessment – represents a promising avenue. However, such tools remain largely absent from routine clinical practice. By targeting the specific biological or structural phenotype, stratified management has the potential to improve therapeutic efficacy, reduce ineffective trial-and-error treatment cycles, and optimize healthcare resource utilization.

The Crucial Role of Patient-Centricity and Research Equity

For multimodal and stratified treatment strategies to succeed, they must be firmly grounded in patient-centered care and guided by the principles of research equity. Meeting patient expectations – particularly regarding functional improvement, pain control, and overall quality of life – is essential. Achieving this requires effective multidisciplinary communication, shared decision-making, and a clear understanding of the patient's knowledge of the disease, personal goals, and values. Equally important is the prioritization of diversity and inclusion throughout all stages of clinical research. This includes representation across different patient populations, socioeconomic backgrounds, genetic ancestries, and geographical regions. The exclusion or underrepresentation of specific demographic groups in clinical trials inevitably leads to therapeutic strategies that are effective for some populations but less effective – or even ineffective – for others.

Therefore, a consistent commitment on equity and diversity in research is not merely an ethical obligation but a scientific necessity. Such an approach ensures that identified phenotypes and resulting therapeutic pathways are robust, generalizable, and applicable across the global OA population, ultimately facilitating the implementation of targeted interventions with meaningful worldwide clinical impact.

Conclusion

In conclusion, the future of osteoarthritis management lies in the adoption of stratified, multimodal therapeutic strategies grounded in patient-centered care and research equity. By embracing these principles, the field can move beyond purely symptomatic management and pave the way for meaningful advances in the personalised treatment of osteoarthritis.

References

1. Reginster JY. The prevalence and burden of arthritis. *Rheumatology* (Oxford). 2002;41 Supp 1:3-6.
2. Neogi T, Zhang Y. Epidemiology of osteoarthritis. *Rheum Dis Clin North Am*. 2013;39(1):1-19.
3. GBD 2021 Osteoarthritis Collaborators. Global, regional, and national burden of osteoarthritis, 1990-2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet Rheumatol*. 2023;5(9):e508-22.
4. Arden NK, Perry TA, Bannuru RR, Bruyère O, Cooper C, Haugen IK, et al. Non-surgical management of knee osteoarthritis: comparison of ESCEO and OARSI 2019 guidelines. *Nat Rev Rheumatol*. 2021;17(1):59-66.
5. Veronese N, Cooper C, Bruyère O, Al-Daghri NM, Branco J, Cavalier E, et al. Multimodal multidisciplinary management of patients with moderate to severe pain in knee osteoarthritis: a need to meet patient expectations. *Drugs*. 2022;82(13):1347-55.
6. Primorac D, Molnar V, Matišić V, Hudetz D, Ječec Ž, Rod E, et al. Comprehensive review of knee osteoarthritis pharmacological treatment and the latest professional societies' guidelines. *Pharmaceuticals* (Basel). 2021;14(3):205.
7. Guthrie B, Thompson A, Dumbreck S, Flynn A, Alderson P, Nairn M, et al. Better guidelines for better care: accounting for multimorbidity in clinical guidelines – structured examination of exemplar guidelines and health economic modelling. *Health Soc Care Deliv Res*. 2017;5(16).
8. Devez LA, Melo L, Yamato TP, Mills K, Ravi V, Hunter DJ. Knee osteoarthritis phenotypes and their relevance for outcomes: a systematic review. *Osteoarthritis Cartilage*. 2017;25(12):1926-41.
9. Mobasheri A, Loeser R. Clinical phenotypes, molecular endotypes and theratypes in OA therapeutic development. *Nat Rev Rheumatol*. 2024;20(9):525-6.
10. Healey EL, Afolabi EK, Lewis M, Edwards JJ, Jordan KP, Finney A, et al. Uptake of the NICE osteoarthritis guidelines in primary care: a survey of older adults with joint pain. *BMC Musculoskelet Disord*. 2018;19(1):295.
11. Heidari S, Babor TF, De Castro P, Tort S, Curno M. Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use. *Res Integr Peer Rev*. 2016;1:2.
12. Abuwa C, Abbaticchio A, Theodorlis M, Marshall D, MacKay C, Borkhoff CM, et al. Identifying strategies that support equitable person-centred osteoarthritis care for diverse women: content analysis of guidelines. *BMC Musculoskelet Disord*. 2023;24(1):734.
13. Cutolo M, Berenbaum F, Hochberg M, Punzi L, Reginster JY. Commentary on recent therapeutic guidelines for osteoarthritis. *Semin Arthritis Rheum*. 2015;44(6):611-7.
14. Mills K, Hübscher M, O'Leary H, Moloney N. Current concepts in joint pain in knee osteoarthritis. *Schmerz*. 2019;33(1):22-9.
15. Berenbaum F. Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis Cartilage*. 2013;21(1):16-21.
16. Donell S. Subchondral bone remodelling in osteoarthritis. *EFORT Open Rev*. 2019;4(6):221-9.
17. Zhu X, Chan YT, Yung PSH, Tuan RS, Jiang Y. Subchondral bone remodeling: a therapeutic target for osteoarthritis. *Front Cell Dev Biol*. 2021;8:607764.
18. Liu W, Guo NY, Wang JQ, Xu BB. Osteoarthritis: mechanisms and therapeutic advances. *MedComm*. 2025;6(8):e70290.
19. Bruyère O, Honvo G, Veronese N, Arden NK, Branco J, Curtis EM, et al. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). *Semin Arthritis Rheum*. 2019;49(3):337-50.
20. Reginster JY, Cooper C, Hochberg M, Pelletier JP, Rizzoli R, Kanis J, et al. Comments on the discordant recommendations for the use of symptomatic slow-acting drugs in knee osteoarthritis. *Curr Med Res Opin*. 2015;31(5):1041-5.
21. Bay-Jensen AC, Henrotin Y, Karsdal M, Mobasheri A. The need for predictive, prognostic, objective and complementary blood-based biomarkers in osteoarthritis (OA). *EBioMedicine*. 2016;7:4-6.
22. Mobasheri A, van Spil WE, Budd E, Uzielienė I, Bernotienė E, Bay-Jensen AC, et al. Molecular taxonomy of osteoarthritis for patient stratification, disease management and drug development: biochemical markers associated with emerging clinical phenotypes and molecular endotypes. *Curr Opin Rheumatol*. 2019;31(1):80-9.
23. Karsdal MA, Rovati LC, Tambiah J, Kubassova O, Ladel C, Berenbaum F, et al. The inflammatory endotype in osteoarthritis: reflections from the 2024 OARSI clinical trials symposium (CTS) with a special emphasis on feasibility for clinical development. *Osteoarthritis Cartilage*. 2025;7(2):100572.
24. Fuggle NR, Chapurlat R, Laslop A, Al-Daghri N, Alokail M, Thiagarajan JA, et al. Novel approaches to the stratified management of knee osteoarthritis. *Nat Rev Rheumatol*. 2025;21(11):684-95.
25. Đukić J, Jevtić M, Bošković K. Influence of the outcome of knee osteoarthrosis treatment on patient. *Med Pregl*. 2023;76(7-8):203-8.

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Anatomy, as a fundamental biomedical discipline, plays a crucial role in understanding the structure and function of the human body, as well as in advancing clinical practice and medical education. The continuous development of morphological sciences and their integration with modern diagnostic and research approaches highlight the importance of scientific meetings as platforms for the exchange of knowledge and experience.

In this context, the Serbian Anatomical Society of Serbia is organizing the **IX Congress with international participation**, which will be held from **September 24 to 26, 2026, at the Faculty of Medicine, University of Novi Sad**. The congress will gather leading experts in anatomy from the region and worldwide, aiming to promote the exchange of the latest scientific findings and to strengthen international collaboration in the field of morphological sciences. It is our great pleasure to announce the arrival of Professor Dr. R. Shane Tubbs, a scientist with over 2,000 publications and the Editor-in-Chief of *Gray's Anatomy*.

The scientific program will include plenary lectures, invited lectures, oral and poster presentations, with a particular focus on clinical and applied anatomy, anatomical variations, and contemporary trends in morphological research. Special attention will be dedicated to young researchers, and the best student paper will be awarded and published in the journal *Medicinski pregled*.

Detailed information on the scientific program, abstract submission, and participation is available on the official congress website: <https://www.drustvoanatoma.com/en/congress.html>

Savremena anatomija, kao fundamentalna biomedicinska disciplina, ima ključnu ulogu u razumevanju strukture i funkcije ljudskog organizma, kao i u unapređenju kliničke prakse i medicinskog obrazovanja. Kontinuirani razvoj morfoloških nauka i njihova integracija sa savremenim dijagnostičkim i istraživačkim pristupima ukazuju na značaj naučnih skupova kao prostora za razmenu znanja i iskustava.

U tom kontekstu, Srpsko anatomsko društvo Srbije organizuje IX Kongres sa međunarodnim učešćem, koji će biti održan na Medicinskom fakultetu Univerziteta u Novom Sadu u periodu od 24. do 26. septembra 2026. godine. Kongres će okupiti vodeće stručnjake iz oblasti anatomije iz zemlje, regiona i sveta, sa ciljem razmene najnovijih naučnih saznanja i unapređenja međunarodne saradnje u oblasti morfoloških nauka. Posebno nam je zadovoljstvo da najavimo dolazak Profesora dr R. Šejn Tabsa, naučnika sa preko 2000 publikacija i glavnog urednika „Gray's Anatomy“.

Naučni program obuhvatiće plenarna predavanja, predavanja po pozivu, usmene i poster prezentacije, sa posebnim osvrtom na kliničku i primenjenu anatomiju, anatomske varijacije, kao i savremene tokove u morfološkim istraživanjima. Posebna pažnja biće posvećena mladim istraživačima, a najbolji studentski rad biće nagrađen "Jolesovom poveljom" i objavljen u časopisu *Medicinski pregled*.

Kongres je akreditovan za lekare, stomatologe i stručnjake srodnih biomedicinskih i morfoloških disciplina, sa 13 bodova za predavače po pozivu, 11 bodova za usmenu prezentaciju, 9 bodova za poster prezentaciju i 7 bodova za slušaoce.

Detaljne informacije o naučnom programu, prijavi radova i registraciji dostupne su na zvaničnoj internet stranici kongresa: <https://www.drustvoanatoma.com/congress.html>