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HALEON HEALTH PARTNER TIMES

for Clinical Practice

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Welcome to the newest series of our scientific newsletter, featuring curated insights at the intersection of clinical reality and evolving evidence. This issue explores timely topics from rational use of nasal decongestants and real-world analgesic experiences to nutrition, bone health, infectious diseases, and the rising global burden of osteoarthritis. Together, these articles highlight how research, when translated thoughtfully, can meaningfully influence patient outcomes.

CLINICAL KEY

Nasal Decongestants & Rebound Congestion: Myths, Facts, and Clinical Reality

MYTH	FACT
Patients become "dependent" on nasal sprays[1]	Symptoms often described as problematic nasal spray use typically reflect recurrence of underlying congestion or administration exceeding labeled recommendations (e.g., >7–10 days), rather than true pharmacologic dependence. Clinical trials show that oxymetazoline, when used as labeled with twice-daily dosing for ≤ 7–10 days, demonstrates sustained efficacy without evidence of dependence, tolerance, or withdrawal[1]
Even a few days of oxymetazoline can trigger RC[1,2]	Multiple randomized controlled trials show no evidence of rebound congestion with short-term use (≤7–10 days). Studies using objective measures such as nasal airway resistance and acoustic rhinometry found no worsening of congestion after treatment discontinuation[1,2]
Intranasal corticosteroids should replace decongestants entirely[1,2]	Short-term combination therapy can offer added benefit. Evidence shows that oxymetazoline plus an intranasal corticosteroid: • Improves nasal airflow and symptom relief and enhances quality of life • Does not increase rebound congestion risk when used appropriately[1,2]

References:
1. Graf P, Enerdal J, Hallén H. Ten days' use of oxymetazoline nasal spray with or without benzalkonium chloride in patients with vasomotor rhinitis. *Arch Otolaryngol Head Neck Surg.* 1999 Oct;125(10):1128-32.
2. Malik M, Gawargi L, Verma A *et al.* No Rebound Congestion with Short-Term Use of Oxymetazoline Hydrochloride Nasal Spray Decongestant. *Journal of Current Medical Research and Opinion.* 5(12), 1520-1529.

Evaluating FUO Origin: Definitions in a Tertiary Care Setting

Why Revisit FUO Now?

FUO has long been defined using rigid criteria fever ≥ 101°F for > 3 weeks without diagnosis. While historically useful, these benchmarks may no longer reflect real-world practice, especially in regions with high infectious disease burden and earlier hospital presentation.

What was Studied?

Over five years (2018–2022), AIIMS Rishikesh evaluated 228 adult FUO cases, applying revised definitions that accounted for:

- Lower fever thresholds (≥ 99.1°F)
- Shorter fever duration (3–21 days)
- Pragmatic hospitalization timelines

What Emerged?

A striking 40.8% of patients fell into a category not captured by classical FUO definitions, while only 2.2% met traditional criteria. This suggests that many clinically relevant FUO cases may be overlooked when older definitions are strictly applied.

What caused FUO?

- Infections dominated, followed by autoimmune diseases and malignancies
- Etiological patterns remained consistent, regardless of how FUO was defined
- **Did Broader Criteria Affect Outcomes?**
  No. Mortality rates and 180-day outcomes weresimilar across all FUO groups, indicating that earlier and broader identification does not compromise patient safety.

Abbreviation: FUO: Fever of unknown origin; AIIMS: All India Institute of Medical Sciences.

Reference: Dhangar P, Panda PK, Kant R, et al. Evaluating fever of unknown origin definitions in a tertiary care setting: Implications for diagnostic criteria revision. *World J Exp Med.* 2025;15(2):101388.

Real time Use of Diclofenac Gel: Patients' experience and utilization patterns

Study Population & Data Strength

- **467** adults evaluated in prospective patient surveys
- **95,085** real-world pharmacy dispensing records analyzed
- Mean age: **60.8** years
- **67.9%** of users were **≥65** years

Baseline Clinical Profile

- Average baseline pain score: **6.0 / 10**
- **74.3%** co-prescribed at least one cardiovascular medication

Pain Reduction Over Time

- **–0.8** point improvement at Week **4**
- **–1.2** point improvement at Week **12**

Functional Outcomes

- Reduction in functional interference across:
  - Daily activities
  - Physical function
  - Social activities

Real-World Utilization Patterns

- **70.8%** dispensed only one tube
- **77.3%** did not switch to another topical therapy or NSAID

Abbreviation: NSAID: Nonsteroidal anti-inflammatory drug.

Reference: Maihöfner C, de Haas A, Sethi V, et al. Patients' experience and utilization patterns of diclofenac gel in Germany: a real-world study with a prospective longitudinal survey and a retrospective analysis of pharmacy data. *Curr Med Res Opin.* 2023;39(12):1649-1661.

Why Multivitamin Supplementation Matters in India?:
Evidence from CENTRIC Observational Study[1,2]

Micronutrient deficiencies remain widespread among Indian adults:

- Vitamin D: up to 97% (99% in those > 60 yrs)
- Vitamin B2: 50%
- Vitamin B6 & B12: ~46%

Multivitamin Use: Common, Yet Under-Studied

- Deficiencies Remain Widespread Among Indian Adults:
- 74% of Indian HCPs are inclined to prescribe multivitamins
- However, self-medication is common (~33% users)
- Users primarily seek benefits for general health, fatigue, and weakness

What This Study Evaluated?

- Multivitamin supplementation in Men, Women, and Adults 50+
- Focus on patient-reported outcomes, including: Health-related quality of life, immune fitness, daily functioning

Exceptional Compliance with Centrum Supplementation

Remarkable adherence with 99% of participants still taking Centrum at follow-up

- Regular use (≥ 3 days per week) was reported by:
  - **97%** of Centrum Men users
  - **92.8%** of Centrum Women users
  - **99.5%** of Centrum Adults 50+ users

Meaningful Improvements in QoL

- After 3 months of supplementation, significant enhancements in overall health-related QoL were observed across all three cohorts
- **EQ-5D Utility Score**
- Statistically significant improvement in mean EQ-5D utility scores in **all groups** compared with baseline
- **Domain-Specific Benefits**
  Reported improvements across all five dimensions: Mobility, self-care, usual activities, pain and discomfort, anxiety and depression

Global Health Perception (EQ-VAS)

- Mean EQ-VAS scores increased significantly from baseline, reflecting better perceived overall health and well-being

Enhanced Immune Fitness with Fewer Sick Days

- Centrum supplementation was linked to measurable improvements in self-reported immune health:

- Immune fitness rating (0–10 scale)
- Centrum Men: 7.0 → 8.9 ($P < 0.001$)
- Centrum Women: 7.0 → 8.7 ($P < 0.001$)
- Centrum Adults 50+: 5.6 → 7.6 ($P < 0.001$)

Reduced Poor Immune Fitness

- A dramatic decline in participants reporting "reduced immune fitness":
- Men: 57.4% → 1.5%
- Women: 47.4% → 1.9%
- Adults 50+: 73.1% → 0.5%

Fewer Sick Days

- Mean sick days decreased substantially in all groups:
- Men: 3.8 → 1.8 days
- Women: 3.8 → 1.9 days
- Adults 50+: 6.0 → 3.0 days

Safety and Tolerability

- No adverse events were solicited or reported during the study.
- Findings suggest excellent tolerability in real-world use

In real-world settings, Centrum multivitamin supplementation demonstrates outstanding compliance, meaningful improvements in QoL, enhanced immune fitness, and excellent safety supporting its role as a reliable foundation for micronutrient adequacy and overall well-being.

Abbreviation: EQ-VAS: EuroQol-visual analogue scale; QoL: Quality of life.

Reference: 1. Shivane V, Sharma A, Bhagat T, *et al*. CENTRIC Observational Study: Effectiveness of Centrum Multivitamin on Quality of Life and Immune Health Parameters in Indian Population. *JCPR*. 2025;21(10).
2. Shivane V, Sharma A, Bhagat T, et al. CENTRIC observational study: effectiveness of Centrum multivitamin supplementation on cognitive function and energy parameters in the Indian population. Int J Pharm Bio-MedSci. 2025;5(9):512–520.

A Quick Read:
Calcium Citrate Malate-A Smarter Calcium Choice

Calcium is a quiet cornerstone of good health, yet for many of us, it remains surprisingly low on the priority list. In today's world, we are surrounded by an endless array of tempting foods and beverages. While convenient and appealing, many of these choices steer us away from naturally calcium-rich foods particularly dairy, which remains under-consumed by those who may need it most. Lactose intolerance, food allergies, vegan diets, or simple personal preference can make traditional calcium sources impractical or inadequate. In such cases, calcium supplementation or fortification of everyday foods and drinks becomes not just helpful but essential.[1]

It's a common misconception that all calcium supplements work the same way. In reality, different calcium salts vary significantly in: Chemical composition, absorption in the body, compatibility with foods and beverages, real health impact. Among these, calcium citrate malate stands out.[1]

Why Calcium Citrate Malate is Special?

Unlike many other calcium sources, calcium citrate malate offers a unique combination of benefits:[1]

- Highly soluble in water making it easier to incorporate into foods and drinks
- Better absorption across age groups
- Works well even in low-acid stomach conditions
- Flexible composition, can be tailored for different formulations
- Tasteless, can fortify foods without changing flavor

Because of these qualities, calcium citrate malate has gained increasing scientific attention since it was first patented in the late 1980s.[1]

Why This Matters?

Choosing the right calcium source isn't just about quantity it's about quality, bioavailability, and real-world effectiveness. While other calcium salts can also serve as fortificants, research continues to highlight the advantages

of calcium citrate malate in supporting bone health and overall wellness.[1]

Quadra Power: Why the Combination Matters?

Quadra Power (Vitamin D3 + Vitamin K2 + Magnesium + Calcium) works as an integrated metabolic system rather than four isolated nutrients. Its strength lies in mechanistic synergy, ensuring that calcium is absorbed, activated, directed to bone, and prevented from depositing in soft tissues.[2]

Core Benefits of Quadra Power[2]

1) Optimizes Calcium Utilization (Not Just Intake)

- Vitamin D3 increases intestinal absorption of calcium, phosphate, and magnesium.
- Magnesium ensures Vitamin D3 is converted to its active form (calcitriol) — preventing "functional Vitamin D resistance."
- Together, they improve true calcium bioavailability, not just serum levels.

2) Promotes Stronger, Better-Quality Bone

Quadra Power supports every step of bone formation[2]:

3) Prevents Misplaced Calcium ("Calcium Paradox")[2]

Step in Bone Formation	Nutrient Responsible	Clinical Impact
Calcium absorption	**Vitamin D3**	More mineral available for bone
Vitamin D activation	**Magnesium**	Enables D3 to actually work
Osteocalcin production	**Vitamin D3**	Stimulates bone-building protein
Osteocalcin activation	**Vitamin K2**	Converts it to carboxylated (active) form
Mineral crystal formation	**Magnesium + Calcium**	Improves bone density & stiffness
Result: Better mineralization, improved bone architecture, and reduced fracture risk.		

Reference: 1. Shivane V, Sharma A, Bhagat T, *et al*. CENTRIC Observational Study: Effectiveness of Centrum Multivitamin on Quality of Life and Immune Health Parameters in Indian Population. *JCPR*. 2025;21(10).
2. Shivane V, Sharma A, Bhagat T, et al. CENTRIC observational study: effectiveness of Centrum multivitamin supplementation on cognitive function and energy parameters in the Indian population. Int J Pharm Bio-MedSci. 2025;5(9):512–520.

High-dose Vitamin D alone can increase calcium flux — which may deposit in arteries instead of bone.

Quadra Power solves this by:

- Vitamin K2 activating Matrix Gla Protein (MGP) → prevents vascular calcification
- Ensures calcium is directed into bone rather than arteries

4) Reduces Risk of Vitamin D Over-Supplementation Complications[2]

With high-dose Vitamin D3:

- Magnesium prevents functional deficiency of active Vitamin D
- Vitamin K2 prevents buildup of undercarboxylated osteocalcin (ucOC)
- This reduces risks of:
  - Hypocalcemia
  - Poor bone mineralization
  - Vascular calcification

5) Supports Bone Remodeling Balance

Quadra Power favorably influences:

- ↓ MMP activity (less cartilage/bone breakdown)
- ↓ Parathyroid hormone (PTH) overactivity
- Balanced osteoblast–osteoclast function
- Better bone turnover profile

References: 1. Reinwald S, Weaver CM, Kester JJ. The health benefits of calcium citrate malate: a review of the supporting science. Adv Food Nutr Res. 2008;54:219-346.2. Maulana, Muhammad. (2025). A Systematic Review and Meta-Analysis of High- Dose Vitamin D3, K2, and Magnesium on Bone Health Outcomes Mechanistic Synergy of Vitamin D3, K2, and Magnesium in Skeletal Metabolism. Available at https://www.researchgate.net/publication/397626950_A_Systematic_Review_and_Meta-Analysis_of_High-_Dose_Vitamin_D3_K2_and_Magnesium_on_Bone_Health_Outcomes_Mechanistic_Synergy_of_Vitamin_D3_K2_ and_ Magnesium_in_Skeletal_Metabolism accessed on January 09, 2026.

INNOVATION CORNER

Can Your Immune System Help Protect Your Cartilage? The Story of Collagen (uDIIC)

Osteoarthritis (OA) is increasingly recognized as a disorder of cartilage degeneration, chronic low-grade inflammation, and immune dysregulation, rather than mere mechanical "wear and tear." Within this evolving paradigm, uDIIC has emerged as a mechanistically rational nutraceutical that targets the immune basis of cartilage destruction rather than providing only symptomatic relief.

Mechanistic Rationale: Oral Tolerance and Immune Reprogramming

Orally administered uDIIC retains its native triple-helical structure, allowing it to reach the small intestine intact, where it interacts with Peyer's patches within gut-associated lymphoid tissue.

Key immunological events include:

- Uptake of uDIIC by dendritic cells via epitope-specific binding
- Antigen presentation through major histocompatibility complex (MHC) complexes to naïve T cells
- Differentiation into regulatory T cells (Tregs)
- Systemic migration of Tregs to inflamed joints

At the joint level, uDIIC-mediated immune modulation results in:

- ↑ IL-10 (anti-inflammatory)
- ↓ IL-1β and IL-6 (pro-inflammatory)
- ↑ TGF-β and type II collagen synthesis (anabolic signaling)

This mechanism underpins a targeted immunomodulatory effect that attenuates autoimmune-driven cartilage degradation, particularly relevant in inflammatory OA phenotypes.

Human Clinical Evidence:

A 24-week prospective study in knee OA (KL grade II–III) using 40 mg/day uDIIC demonstrated:

Clinical Outcomes

- WOMAC ↓ 33.1%
- Lequesne Index ↓ 25%
- Significant improvement noted as early as week 4

Structural Outcomes

- Ultrasound showed increased femoral cartilage thickness in both knees

Biochemical Markers

- Initial rise in urinaryC-telopeptide of type II collagen (CTX-II) (likely remodelingphase)
- Subsequent decline by week 12 → reduced cartilage catabolism

Medication-Sparing Effect

- 30% of baseline NSAID users discontinued Nonsteroidal anti-inflammatory drug (NSAID) during the study

Safety

- No adverse drug reactions reported
- Well tolerated over 6 months

Interpretation: uDIIC demonstrates features of a potential disease -modifying osteoarthritis agent (DMOAD adjunct) rather than merely symptomatic therapy.

Why UC-II® Merits Attention?

Among the limited human studies available, six key publications utilized UC-II® (Lonza, USA) and consistently reported:

- Reduced systemic inflammation
- Improved joint function
- Favorable cartilage biomarkers
- Reproducibility across preclinical and clinical settings

Reference: Bhagat T, Sharma A, Narang P, Mukherjee AN, Ravi Kumar YS. Clinical prospects of undenatured type II collagen: A novel approach in osteoarthritis management. *Int J Orthop Sci.* 2025;11(4):95-102.

Osteoarthritis: Beyond Symptom Control to Disease Modification

Why OA Progresses?

Cartilage degeneration driven by chondrocyte dysfunction

- Subchondral bone remodeling with osteophyte formation and sclerosis
- Synovial inflammation, a key source of pain and tissue damage
- Oxidative stress and protease activity accelerating matrix breakdown
- Epigenetic dysregulation, altering inflammatory and catabolic pathways

Treatment Landscape

- While NSAIDs and acetaminophen remain mainstays for pain relief, emerging strategies—biologics, regenerative medicine, epigenetic therapies, and molecular targets, aim to modify disease progression. However, no single approach has yet delivered sustained joint protection.

Looking Ahead

- Future osteoarthritis care lies in multi-target therapies, precision medicine, and regenerative approaches, supported by advances in drug delivery and long-term clinical validation.

Reference: Dell'Isola A, Recenti F, Giardulli B, *et al.* Osteoarthritis year in review 2025: Epidemiology and therapy. *Osteoarthritis and Cartilage.* 2025 Sep 4.

Recent Advances and Gaps in Therapeutics for Severe Fever with Thrombocytopenia Syndrome Virus (SFTSV) - 3 Wins, 3 Barriers, 3 Priorities

3 KEY WINS

- Favipiravir and VV261 inhibit viral replication
- Calcium channel blockers prevent viral entry
- SNB02 nanoantibody advances to clinical trials

3 MAJOR BARRIERS

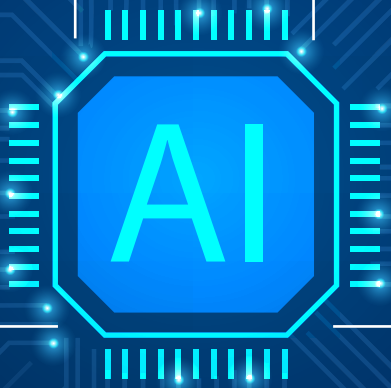
- Single-target focus
- Drug resistance risk
- SNB02 nanoantibody advances to clinical trials

3 RESEARCH PRIORITIES

- Multi-target combination therapies
- Viral replication pathway mapping
- Next-generation drug delivery systems

Reference: Dang H, Wang Y, Zhang L, et al. Recent Advances in Therapeutics for Severe Fever with Thrombocytopenia Syndrome Virus. Viruses. 2025;17(9):1174.

ADVANCES IN DIAGNOSTIC TECHNOLOGIES FOR ALLERGIC RHINOSINUSITIS



Molecular testing

- **Specific applications:** Genetic polymorphism analysis (ZNF608)
- **Advantages:** Personalized risk assessment
- **Clinical impact:** Precision medicine approaches

Advanced imaging

- **Specific applications:** High-resolution CT, functional MRI
- **Advantages:** Enhanced anatomical detail
- **Clinical impact:** Improved surgical planning

Point-of-care tools

- **Specific applications:** Rapid allergen testing, digital biomarkers
- **Advantages:** Immediate results, convenience
- **Clinical impact:** Faster diagnosis and treatment

Digital monitoring

- **Specific applications:** Wearable biosensors, smartphone apps
- **Advantages:** Continuous data collection
- **Clinical impact:** Real-time symptom tracking

AI-driven diagnosis

- **Specific applications:** Machine learning algorithms, pattern recognition
- **Advantages:** Improved accuracy, standardization
- **Clinical impact:** Enhanced diagnostic precision

Reference: Addissouky TA. Recent advances in allergic rhinosinusitis management: from traditional therapies to precision medicine. The Egyptian Journal of Otolaryngology. 2025 Dec;41(1):1-2.