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New Alzheimer's Study Raises Questions About Glucosamine: Why the IOM Nutrient Prioritization Principle Matters

By Richard Z. Cheng, MD, PhD
Editor-in-Chief, Orthomolecular Medicine News Service (OMNS)

Highlights

- Could glucosamine accelerate Alzheimer's disease progression? A new study raises important questions.
- For joint and bone health, is glucosamine truly necessary-or are more fundamental nutritional and metabolic factors being overlooked?
- The IOM Nutrient Prioritization Principle provides a practical framework for deciding what nutritional interventions should come first.

A New Study Raises Questions About Glucosamine

A recently published study in *Nature Metabolism* reported that glucosamine supplementation accelerated Alzheimer's disease progression in mouse models and was associated with worse outcomes among patients with dementia. [1]

The study quickly attracted attention because glucosamine is one of the world's most widely used dietary supplements, commonly taken for joint health.

However, the most important lesson from this study may not be about glucosamine itself.

Rather, it highlights a larger issue that is often overlooked in nutrition and supplement discussions: not **all nutrients and supplements deserve equal priority**. The **IOM Nutrient Prioritization Principle**, recently proposed as a systems framework for nutritional intervention [5], provides a practical method for distinguishing foundational nutritional and metabolic needs from supportive and optimization strategies.

What the New Study Found

Researchers identified a phenomenon they called **hyperglycosylation** in Alzheimer's disease.

In mouse models:

- Increased glycosylation was associated with worse cognitive function.
- Reducing glycosylation improved memory performance.
- Glucosamine supplementation increased glycosylation and worsened cognitive outcomes.

The investigators also analyzed electronic health records from patients with dementia and reported an association between glucosamine use and:

- Higher mortality
- Faster progression from mild cognitive impairment (MCI) to dementia

These findings are intriguing and deserve further study.

However, several important limitations should be noted.

Association Is Not Causation

The human portion of the study was observational rather than a randomized clinical trial.

Therefore, the findings demonstrate an association but do not prove that glucosamine causes dementia.

Importantly, some previous population studies have reported the opposite association, suggesting potential benefits among glucosamine users.

The overall evidence remains mixed, and further research is needed.

The Bigger Question: Where Does Glucosamine Belong?

Regardless of whether the proposed mechanism ultimately proves clinically important, the study raises a broader practical question:

Where should glucosamine fit within an overall nutritional strategy?

This is where many consumers become confused.

Modern supplement markets contain thousands of products, including:

- Vitamins
- Minerals
- Amino acids
- Herbal extracts
- Antioxidants
- Mitochondrial supplements
- Longevity compounds
- Countless specialty nutrients

Consumers are often led to believe that newer and more specialized supplements are automatically better.

In reality, physiology does not work that way.

This is where the **IOM Nutrient Prioritization Principle** may provide a useful framework.

The IOM Nutrient Prioritization Principle

The IOM Nutrient Prioritization Principle provides a simple systems-based framework for nutritional decision-making [5].

As illustrated in Figure 1 (adapted from [5]), nutritional interventions can be broadly organized into four levels:

1. Foundational & Orthomolecular Nutrition
2. Increased-Demand Nutrients
3. Therapeutic Nutritional Interventions
4. Optimization & Emerging Strategies

The hierarchy reflects a central principle:

Foundation Before Optimization

The goal is not to discourage the use of specialized supplements. Rather, it is to place them in their proper context.

Nutritional and metabolic foundations should be addressed first. Increased physiological demands should be recognized and supported. Therapeutic nutritional interventions may be used when clinically appropriate. Optimization and longevity-oriented strategies can then be considered after these foundational needs have been met.

From an IOM perspective, glucosamine is best viewed as a supportive supplement rather than a foundational nutritional requirement.

The more important question is not whether glucosamine works.

The more important question is:

Where does glucosamine belong within an overall health strategy?

Figure 1. The IOM Nutrient Prioritization Principle (adapted from [5]).

IOM NUTRIENT PRIORITIZATION PRINCIPLE

FOUNDATION BEFORE OPTIMIZATION

IOM Systems Medicine
Orthomolecular Medicine for the 21st Century

Focus on what your body needs most—first.
Build a strong foundation, then optimize.

HIGHER PRIORITY

LEVEL 1 — FOUNDATIONAL & ORTHOMOLECULAR NUTRITION

Build the nutritional foundation.
Correct deficiencies and achieve optimal nutrient status.

Examples:

- **All Vitamins** (especially Vitamin C, Vitamin D, B Vitamins)
- **Essential Minerals** (especially Magnesium, Zinc, Selenium)
- **Healthy Fats** (especially Omega-3 fatty acids)
- **Quality Protein**

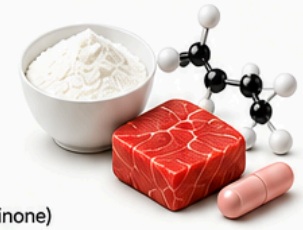
LEVEL 2 — INCREASED-DEMAND NUTRIENTS

Requirements increase with aging, stress, illness, recovery, or chronic disease.

(Reflecting the IOM Nutrient Demand Principle)

Examples:

- Taurine
- Glycine
- Glutamine
- Creatine
- CoQ10 (Ubiquinone)



LEVEL 3 — THERAPEUTIC NUTRITIONAL INTERVENTIONS

Use nutrition as a therapeutic tool for specific conditions.

This may include therapeutic use of foundational nutrients at high or orthomolecular doses.

Examples:

- High-dose Vitamin C (HDIVC)
- High-dose Vitamin D (autoimmune protocols)
- High-dose Niacin
- Therapeutic Omega-3
- NAC (N-Acetyl Cysteine)
- Glutathione
- Alpha-Lipoic Acid (ALA)

LEVEL 4 — OPTIMIZATION & EMERGING STRATEGIES

For further optimization of health, resilience and longevity.

Examples:

- Polyphenols
- Probiotics
- Adaptogens
- PQQ
- NMN / NR
- Spermidine
- Urolithin A
- Other emerging longevity strategies

LOWER PRIORITY

CORE PRINCIPLE | Foundation Before Optimization. Build the foundation first.

DON'T DO THIS

= D Mg C

Deficiencies in Basic Nutrients

Skipping the basics weakens your foundation.

DO THIS

Foundation — Build the basics first → **Support** — Meet higher demands → **Therapy** — Use targeted nutrition → **Optimization** — Enhance health & longevity

Foundation Before Optimization

The central principle is simple:

Build the foundation first.

Before pursuing increasingly specialized interventions, nutritional and metabolic foundations should be addressed first.

From an IOM perspective, glucosamine is best viewed as a targeted supportive supplement rather than a foundational nutritional requirement.

The more important question is not whether glucosamine works.

The more important question is:

Where does glucosamine belong within an overall health strategy?

Do We Really Need Glucosamine for Joint Health?

The purpose of the IOM Nutrient Prioritization Principle is not to discourage the use of glucosamine or other supportive supplements.

Rather, it is to place them in their proper context.

Before asking whether glucosamine is beneficial, it may be worth asking a more fundamental question:

Are the nutritional, metabolic, and lifestyle foundations for joint health already in place?

For bone and joint health, IOM Systems Medicine emphasizes addressing foundational physiological requirements first.

Core Nutritional Foundations

- Vitamin C

- Vitamin D
- Magnesium
- Vitamin K2
- Adequate protein intake
- Essential fatty acids

These nutrients play important roles in:

- Collagen synthesis
- Connective tissue integrity
- Bone matrix formation
- Mineral metabolism
- Muscle function
- Inflammation regulation

Metabolic and Lifestyle Foundations

Equally important are:

- Healthy body weight
- Regular physical activity
- Resistance training
- Adequate sleep
- Metabolic health
- Low-carbohydrate and ketogenic dietary strategies
- Avoidance of smoking
- Minimizing ultra-processed foods

From an IOM perspective, osteoporosis and degenerative joint disease are rarely the result of a single nutrient deficiency.

They are usually manifestations of broader disturbances involving nutrition, metabolism, inflammation, hormonal balance, connective tissue integrity, and aging-related physiological decline.

In IOM Systems Medicine, the goal is not to find a single "magic supplement" for bone or joint health.

The goal is to create the biological conditions that allow tissues to maintain, repair, and regenerate themselves as effectively as possible.

A Personal Perspective: Foundations Before Supplements

This discussion of glucosamine brings to mind a personal experience.

Nearly 20 years ago, when I first started playing badminton, I had persistent right shoulder pain and knee soreness when climbing stairs.

Around the same time, I adopted a low-carbohydrate ketogenic diet, practiced intermittent fasting, and focused on foundational nutrition, including vitamin C, vitamin D, magnesium, omega-3 fatty acids, and mitochondrial-support nutrients.

Notably, I never took pain medications, glucosamine, or other joint supplements.

Over time, my shoulder pain disappeared, and my knee discomfort resolved.

Today, at age 66, I continue to play badminton three to four times per week, often for two to three hours at a time. I regularly compete with players 20 to 40 years younger and maintain excellent mobility and endurance.

While anecdotal, this experience illustrates an important principle of IOM Systems Medicine.

Rather than focusing on a single supplement for a single symptom, I focused on improving the body's overall physiological environment.

The goal was not simply to reduce joint pain, but to improve the body's capacity to maintain, repair, and regenerate itself.

This experience reinforced my belief that foundational nutrition and metabolic health should come first.

In many cases, restoring the foundation may matter more than finding the perfect supplement.

The Bottom Line

The glucosamine study raises important scientific questions and deserves further investigation.

However, its greatest value may lie elsewhere.

It reminds us that nutritional interventions should be prioritized according to biological importance rather than marketing popularity.

The goal of nutritional medicine is not to take more supplements.

The goal is to identify which interventions matter most.

Before asking whether a specialized supplement is beneficial, it may be worth asking a more fundamental question:

Have the nutritional, metabolic, and lifestyle foundations already been addressed?

In IOM Systems Medicine, the guiding principle is simple:

Foundation Before Optimization

The right supplement at the wrong priority level may provide little benefit.

The right foundation, however, often changes everything.

Acknowledgment

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