



# Research Summary: Nitric Oxide #1

As featured in Dr. Kenny Mittelstadt's video:  
"What Is Nitric Oxide & How to Make More Nitric Oxide in Your Body?"  
Date of Publication: 03/03/2026

## Research Context:

This week's topic explores nitric oxide as more than a trendy supplement ingredient or athletic performance enhancer. Nitric oxide is a foundational signaling molecule that allows your blood vessels to relax, helps regulate blood pressure, supports oxygen delivery, and influences metabolic health.

When nitric oxide signaling declines, circulation becomes less adaptable. Blood vessels may stiffen. Blood pressure may creep upward. Glucose regulation can shift. Energy delivery to tissues can become less efficient. These changes often happen gradually, long before a formal diagnosis appears.

Nitric oxide production depends on multiple inputs. Your oral microbiome helps convert dietary nitrates into usable nitric oxide precursors. Your food choices determine how much nitrate substrate is available. Your movement patterns stimulate nitric oxide production through your vascular lining.

## Key Findings from the Research:

### Study 1 (PMID 355749621):

Researchers examined 764 adults to evaluate whether certain oral bacteria support nitrite generation, which is a key step in nitric oxide formation, or instead deplete it. They found that people whose oral microbiome showed a higher capacity to generate nitrite relative to breaking it down had better cardiometabolic profiles. A one standard deviation higher nitrite generation-to-depletion ratio was associated with a lower composite cardiometabolic risk score. This score included measures related to blood pressure, glucose metabolism, and other metabolic indicators. Higher levels of ammonia-producing gene activity, which suggests nitrite depletion, were associated with worse cardiometabolic risk. In practical terms, oral bacteria that favor nitric oxide production were linked to healthier metabolic patterns.

### Study 2 (PMID 35369064):

This systematic review and meta-analysis included seven randomized clinical trials with 218 participants diagnosed with hypertension. Researchers evaluated whether nitrate-rich beetroot juice lowers blood pressure. Across intervention periods ranging from 3 to 60 days, systolic blood pressure decreased by approximately 4.95 mmHg on average. Even a reduction of about 5 mmHg in systolic pressure is associated with meaningful cardiovascular risk reduction at a population level. Diastolic blood pressure did not change significantly.

### Study 3 (PMID 36267589)

This meta-analysis evaluated the effect of exercise training on nitric oxide and its circulating metabolites, nitrate and nitrite, often grouped as NOx. Ten randomized controlled trials were included in the pooled analysis. Exercise significantly increased nitric oxide-related markers compared to control groups. This effect was seen with aerobic training, high-intensity interval training, shorter programs lasting eight weeks or less, longer programs exceeding eight weeks, and sessions of varying length. The increase was consistent across different populations and study designs, suggesting that regular movement reliably enhances vascular nitric oxide production regardless of training style or program structure.



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## Functional Medicine Connections:

Nitric oxide functions as a signaling molecule that tells your blood vessels when to relax. That relaxation supports circulation, oxygen delivery, and metabolic flexibility.

Your body produces nitric oxide through two main pathways. One pathway depends on enzymes in the lining of your blood vessels. The other depends on the nitrate-to-nitrite conversion process, which relies heavily on oral bacteria.

The first study highlights a commonly overlooked connection. Changes in the oral microbiome may influence nitric oxide availability. This creates a direct systems link between oral ecology and cardiometabolic health.

The second study shows that dietary nitrates provide the substrate needed for this pathway. The third study shows that exercise stimulates nitric oxide production through vascular adaptation.

Nitric oxide production reflects overall system alignment. When oral ecology, nutrition, and movement patterns support nitric oxide signaling, vascular communication improves. When those inputs decline, nitric oxide availability can gradually decrease.

This is not about a single intervention. It is about how multiple systems interact over time.

## Practical Reflections & Takeaways:

Consider your own patterns. Do you regularly use strong antibacterial mouthwash that may disrupt nitrate-converting bacteria? Is your diet low in leafy greens or other naturally nitrate-rich vegetables? Has your movement routine declined due to stress, schedule changes, or energy shifts?

Nitric oxide levels rarely change overnight. They reflect accumulated inputs. Oral ecology, food quality, and physical activity quietly shape vascular communication over time. When those inputs drift, circulation often becomes less adaptable before symptoms are obvious.

You may not feel nitric oxide directly. Instead, you might notice gradual changes such as rising blood pressure, colder hands and feet, reduced exercise tolerance, or slower recovery. These are not random shifts. They can represent early changes in how efficiently your vascular system responds to demand.

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