



LINUS PAULING INSTITUTE

DIGITAL DIGEST

WINTER/SPRING 2024

LOOKING BACK AT DIET AND OPTIMUM HEALTH 2023 SEE INSIDE ►

AGING WELL & OPTIMUM HEALTH

Exploring the Research on Micronutrients and Healthy Aging

On December 13, 2023, Dr. Emily Ho presented the webinar *Aging Well & Optimum Health: The Role of Micronutrients*. She highlighted the Institute’s approach to healthy aging and the scientific data that inform the Institute’s vitamin and mineral recommendations. A synopsis of that presentation follows, including a brief discussion of the micronutrient studies that Dr. Ho reviewed.

Audience members had many more questions than Dr. Ho could answer in the one-hour webinar. Answers to select audience questions can be found on page 5. A recording of the presentation and Q&A session is available on our YouTube channel.

A Role for Micronutrients in Older Adults

It’s no secret that vitamins and minerals are essential for health. If you are severely deficient in any one of these micronutrients, you run the risk of immediate and serious health consequences. Nowadays, however, severe deficiencies are usually avoidable and rare in the United States.

More common are the subtle shortfalls. This is where people do not reach the recommended amounts of certain vitamins or minerals but have no obvious or immediate health problems. At the Institute, we believe that a lifetime of more subtle micronutrient inadequacies leads to poor health in the long term and drive the development of age-related diseases.

Reaching optimum vitamin and mineral status provides long-term benefits for health and vitality. We refer to this as increasing our healthspan – living longer, better lives.

IN THIS ISSUE

Aging Well & Optimum Health.....1

From the Director....2

Micronutrient Information Center Updates.....3

Aging Well Q&A Follow-Up.....5

Precision Health: Living Better, Longer.....6



Oregon State University
Linus Pauling Institute

Continued on page 4

Photo credit: Karl Maasdam



Emily Ho, PhD
Endowed Chair and Director,
Linus Pauling Institute

FROM THE DIRECTOR

I hope that your year is off to a great start!

At the Institute, the start of a new year means hosting Linus Pauling Day. This is our annual celebration of the Linus Pauling legacy that we hold each year on Dr. Pauling's birthday, February 28. Part of this event included an open house at the Linus Pauling Science Center in Corvallis, Oregon.

We also held our first webinar of the year on Linus Pauling Day, hosting Dr. Francesco Visioli from the University of Padua in Italy. In his presentation, he spoke about the foods, micronutrients, and phytochemicals that make up the Mediterranean diet and the science behind their health benefits.

Dr. Visioli is a long-time friend of the Institute, having spent a couple of summers here in Oregon working with several LPI investigators, their students, and our staff. During his recent acceptance speech for the Federation of European Nutrition Societies Award (a very high honor!), he called his time at the LPI one of the best experiences of his life.

You can access the recording of Dr. Visioli's webinar *Living Better, Longer: Healthy Compounds Found in a Mediterranean Diet* on YouTube at the link below. We will have more of the Q&A from this webinar in the next issue of the *Digital Digest*.

Please note that our annual day of giving, known as **Dam Proud Day**, is fast approaching. We can use your help to support our Healthy Aging Research Fund. We are also seeking support for our flagship outreach program, the Micronutrient Information Center. See more about Dam Proud Day on the back cover.

Part of this initiative involves a partnership with OSU's Division of Research and Innovation to support student research fellows within the Institute. Stay tuned to learn how you can help these students in the next issue of the *LPI Research Newsletter*.

Hope you enjoy this issue. As always, thank you so much for your support!

FRANCESCO VISIOLI, PHD
University of Padua,
Italy

LIVING BETTER, LONGER
Healthy Compounds Found in a Mediterranean Diet

Now online at: lpi.pub/MedDiet2024

Oregon State University
Linus Pauling Institute

MICRONUTRIENT INFORMATION CENTER UPDATES

Folate Article Updates

- **Folate and Homocysteine:** A high blood level of homocysteine is a risk factor for several types of cardiovascular disease. Of the vitamins involved in homocysteine metabolism, folate status appears to have the greatest impact. Recent studies suggest that folic acid supplementation, along with vitamin B₆ and vitamin B₁₂, may help prevent stroke, especially in those with existing cardiovascular disease.

High blood levels of homocysteine are also a risk factor for cognitive decline, dementia, and Alzheimer's disease. There is limited evidence that folic acid supplementation improves cognitive function, although more randomized controlled trials are needed. It is nevertheless prudent to ensure adequate intakes of folate and other B vitamins throughout life for overall health.

- **Supplemental Forms:** Folic acid is the most common form of folate supplement. Many years of clinical trial evidence show that folic acid supplementation supports healthy folate status in the body. Other forms of folate are available as supplements. However, despite claims by manufacturers, there is very little clinical evidence that they are superior to folic acid.

Vitamin B₁₂ Article Updates

- **Vitamin B₁₂ Status:** Although measuring blood concentrations of vitamin B₁₂ (cobalamin) alone is useful, other blood markers may better describe vitamin B₁₂ status. Elevated blood concentration of methylmalonic acid is the specific indicator of vitamin B₁₂ deficiency, but blood concentrations of total cobalamin, holo-transcobalamin (also called "active vitamin B₁₂"), and homocysteine can also be used. Since there is no "gold standard" blood test, the manifestation of clinical symptoms is important in the diagnosis of vitamin B₁₂ deficiency.
- **Who Might Need Supplements:** Anyone who avoids animal products, such as vegans and vegetarians, is at high risk for vitamin B₁₂ deficiency. While fortified foods (e.g., cereals, nutritional yeast) may be a source of the vitamin, it is generally advised that vegans and vegetarians take vitamin B₁₂ supplements.

Additionally, older adults are at increased risk for vitamin B₁₂ deficiency due to typically undetected inflammation in the stomach lining and the resulting decrease in stomach acid production. The use of antacids or other drugs that lower stomach acid also can reduce the absorption of vitamin B₁₂ from food. The use of metformin, which is most commonly prescribed to treat diabetes, can also reduce vitamin B₁₂ absorption. Because low vitamin B₁₂ status is common among older adults, the Institute recommends that all older adults get 100 to 400 µg of vitamin B₁₂ per day from supplements.

- **Supplemental Forms:** Cyanocobalamin is the main form of supplemental vitamin B₁₂ available in the US. Hydroxycobalamin is a form of vitamin B₁₂ commonly used in Europe. Other forms of vitamin B₁₂ include methylcobalamin and adenosylcobalamin.

Sublingual vitamin B₁₂ (placed under the tongue until dissolved) is also available over the counter in the United States. A few studies suggest that the use of sublingual cyanocobalamin or methylcobalamin are effective at increasing vitamin B₁₂ status. 

The full text of the article on folate can be found at: lpi.pub/MIC-folate

Information about high homocysteine levels can be found at: lpi.pub/MIC-HCys

The full text of the article on vitamin B₁₂ can be found at: lpi.pub/MIC-B12

While the Institute focuses on ways to extend healthspan with good nutrition, we recognize that current science cannot yet define optimum levels of micronutrients for each person. However, the Institute continues to conduct nutrition trials in both animals and people towards this effort.

Dr. Ho selected a few of those trials to summarize in her presentation. The first was a preclinical trial conducted by her research group, showing how zinc status influences inflammation in older mice. Older animals that consumed a diet low in zinc had much higher levels of inflammatory biomarkers than young mice that consumed the same diet.

However, older mice that received a diet supplemented with zinc fared much better: inflammatory markers decreased, and other aspects of the immune system improved. This suggests that these older animals had an undetected need for more zinc, which may also be present in older people.

Recent clinical trials have also made progress toward a better understanding of how multivitamins support the nutritional status of older adults. Dr. Ho discussed two studies led by investigators at the Institute, Drs. Adrian Gombart and Tory Hagen.

Dr. Gombart's trial focused on immune function in men and women over the age of 55. Half of the study participants took an immune-focused multivitamin supplement that was high in vitamin C, while the other half took a placebo control.

At the end of the 12-week study, the individuals taking the multivitamin showed increased blood levels of vitamin C and zinc compared to those in the control group. Although both groups reported having respiratory illnesses throughout the study, participants in the multivitamin group reported less severe illness and shorter duration of illness when compared to the control group.

These results suggest that immune response was somehow improved by supplementation, although determining the specific mechanism requires further investigation.



Dr. Hagen's trial focused on metabolism in older men, primarily over the age of 70. Like Dr. Gombart's study, half the study participants took a multivitamin supplement every day, while the other half took a placebo control. The supplement was a multivitamin designed for older men, containing most vitamins and minerals and some phytochemicals.

At the end of the six-month study, participants in the multivitamin group showed significant increases in blood levels of several vitamins, especially vitamin B₆, vitamin D, and vitamin E.

Interestingly, a decline in cellular oxygen consumption was observed in white blood cells obtained from individuals in the placebo group, which was not seen in the multivitamin group. This suggests that the supplement protected the multivitamin group from the decreases in mitochondrial function that occurred in the placebo group.

Dr. Ho expressed that these studies are just the beginning of our research that will help us understand the roles of micronutrients in healthy aging. 🌱

References:

Wong et al. *J Nutr.* **139** (2009);
doi: 10.3945/jn.109.106021

Fantacone et al. *Nutrients* **12** (2020);
doi: 10.3390/nu12082447

Michels et al. *Nutrients* **15** (2023);
doi: 10.3390/nu15122691

A summary of Dr. Gombart's study can be found in the Winter 2021 edition of the *LPI Research Newsletter*.

A more detailed overview of Dr. Hagen's study can be found in the Fall 2023 edition of the *LPI Research Newsletter*.

AGING WELL Q&A FOLLOW-UP

More Audience Questions Answered From Dr. Ho's Webinar

NHANES data show that many adults don't meet potassium intake recommendations. Why is this the case?

Put simply, 80% of children, teens, and adults in the United States are not eating enough fruit and vegetables every day. For example, adults average only 1½ servings of vegetables and only 1 serving of fruit each day, which is far below the goal of 5-7 servings of fruit and vegetables every day.

Most Americans need to dramatically increase fruit and vegetable intake in order to reach potassium intake recommendations of 2,600 mg/day for women and 3,400 mg/day for men. While fruit and vegetables are the primary sources of potassium in the diet, some dairy products like yogurt and seafood are also good sources.

Using dietary supplements to meet your potassium needs is not recommended for several reasons, including the risk of serious side effects.

Dr. Ho indicated that taking too much zinc can interfere with copper absorption. If we decide to take a zinc supplement, is it important to also take a copper supplement?

Taking too much zinc can indeed interfere with copper absorption, but this only occurs when copper and zinc are present in the digestive system at the same time. If you take a zinc supplement, you can still absorb copper from food if you do not take the zinc supplement with copper-rich food sources, such as shellfish, seeds, nuts, and mushrooms. A copper supplement is not necessary.

Adults should limit their zinc intake to 40 mg per day to avoid these issues. Make sure to account for the amount of zinc you are getting from both food and supplements.

Where can we find the Institute's recommendations for vitamins and minerals?

The Institute's Micronutrient Information Center is the best source for this information. Intake recommendations can be found in articles on specific vitamins or minerals and in articles that focus on specific life stages (older adulthood, pregnancy, and childhood).

In addition, you can check out the *Micronutrients for Health* handout on our website.

In the trials using multivitamins, the data for blood serum or plasma were shown. Were the cellular levels of the nutrients also tested?

For most vitamins and minerals, no. This is because in most cases, the plasma levels are considered to be the best indicator of vitamin status. The exception is folate because red blood cell levels of that vitamin are considered a more useful marker of folate status.

An analysis of red blood cell mineral status could be done if additional funding is made available. In theory, micronutrients can also be measured in white blood cells, but these cells can be difficult to obtain in sufficient quantities for testing.

In all of the reviewed studies, it was noted that blood levels of many minerals are not very helpful for assessing nutrient status. Why is that?

Our bodies regulate blood levels of minerals to avoid imbalances that could impact bodily functions. When blood levels increase, our body either stores the extra minerals in tissues or eliminates any excess in urine. When blood levels fall, our body accesses those extra minerals from our tissues and limits urinary excretion to keep blood levels steady. Typically doctors use blood levels of minerals as an indicator of organ function, not nutritional status.

For example, if our body senses that it is not getting enough calcium from the diet, it will take calcium from our bone stores and also limit calcium loss in the urine. During that process, blood calcium levels remain within the normal range, but calcium stores are slowly depleting. Only when the calcium stores are nearly exhausted do blood levels start to drop.

Are there any home tests that we can use to measure our vitamin and mineral levels?

Although many companies claim that they can accurately assess your vitamin and mineral levels through at-home tests, the scientific evidence supporting their use is lacking.

The best tests still require a medical or research lab. Speak to your healthcare provider if you are interested in micronutrient testing. 🌐

PRECISION HEALTH: LIVING BETTER, LONGER

The 2023 Diet and Optimum Health Conference

The Linus Pauling Institute's biennial conference was held on September 19 and 20, 2023 in Corvallis, Oregon. This scientific meeting focused on the theme of precision health and explored the latest advances that exist at the convergence of personalized nutrition and healthspan research.

The conference covered a wide spectrum of nutrition research, including the emerging role of data science, new biomarkers for health, and interventions that promote healthy aging.

Below is an overview of the keynote panel sessions that began each day of the meeting.

Precision Nutrition Keynote Panel

Speakers: Cindy Davis (USDA), Holly Nicastro (NIH), and Andrea Wong (CRN)

This panel fostered a discussion on measuring individualized nutritional needs. All of the panel members agreed that this is a much-needed approach to advance nutrition science, as general dietary recommendations often fall short. Each speaker brought different perspectives on an individualized approach to nutrition and encouraged the use of different tools, technologies, and techniques.

Dr. Holly Nicastro spoke about the *All of Us* research program from the National Institutes of Health (NIH). The goal of this program is to nurture long-term relationships with one million or more participants of diverse backgrounds from across the United States and to create a large biomedical dataset for health research. In this voluntary program, people provide information about their health and habits, biological samples, and access to their electronic health records.

Dr. Cindy Davis discussed food and nutrition research priorities at the United States Department of Agriculture (USDA). These included how food is produced, the effects of food processing, assessing the nutritional value of foods, and how well various nutritional needs are met. She noted that the USDA's Agricultural Research Service maintains FoodData Central, a publicly accessible web tool that provides current nutrition information about a wide variety of foods.

Dr. Andrea Wong from the Council for Responsible Nutrition (CRN) – a trade organization for the dietary supplement and functional food industries – gave an industry perspective. She discussed new tools and technologies that companies use to assess a person's nutritional needs and the effects of dietary supplementation. Such approaches have led to new scientific discoveries that are shared with the public.



Dr. Holly Nicastro, Coordinator for the Nutrition for Precision Health Program at the National Institutes of Health, provides an overview of the *All of Us* research program.



Dr. Bruce Y. Lee, Professor at the City University of New York, talks about the potential for AI and other technologies to inform approaches to personalized nutrition.



The Young Investigator Award finalists pose with Drs. Emily Ho and Maret Traber from the LPI (left) and Dr. Eric Ciappio from the Balchem Corporation (right).

Healthspan Research Keynote Panel

Speakers: Matt Kaeberlein (Optispan), Holly Van Remmen (OMRF), and David Furman (Buck Institute)

This panel discussion centered around maximizing the healthy period of our lives and delaying the declines associated with aging. Each panel member highlighted a slightly different approach.

Dr. Matt Kaeberlein is the founding director of the University of Washington's Healthy Aging and Longevity Research Institute and the CEO of Optispan. He spoke about the need to separate fact from fiction in the field of aging, including pushing back against current fads like calorie-restrictive diets, intermittent fasting, and the use of aging "clocks."

Dr. Holly van Remmen is a professor at the Oklahoma Medical Research Foundation (OMRF), where her research focuses on frailty – a common problem for adults of advanced age. She spoke about the involvement of mitochondrial dysfunction in muscle wasting that occurs with aging and the need for additional study in this area. It is possible that targeting therapeutics to the mitochondria may be one key to reverse this decline.

Dr. David Furman is an Associate Professor and Director of the Bioinformatics Core at the Buck Institute for Research on Aging and co-founder of Edifice Health, Inc. His work seeks to use artificial intelligence technologies to integrate the interpretation of various blood markers into an easy-to-understand health score and develop it as a marker of biological age. Edifice uses this score to provide its clients with a summary of their immune system and actionable interventions to reduce inflammation and – ideally – the risk for disease. 🌐



Philenroza Thavrin, a student researcher from the Stevens laboratory at the LPI, presents her poster on the impacts of intravenous vitamin C in cancer patients.

Other Sessions of Diet and Optimum Health 2023:

- How Big Data Informs Optimal Nutrition
- Nutrition and the Microbiome
- Healthy Aging Interventions
- Fortifying an Aging Immune System
- Slowing the Decline: Healthy Cognitive Function with Age

More information about all of these sessions can be found on the Diet and Optimum Health conference website.



Evidence for New Vitamin C Recommendations?

One of our invited speakers was Dr. Anitra Carr from the University of Otago, Christchurch. Dr. Carr's presentation focused on factors that influence vitamin C concentrations in the body. She and her colleagues examined vitamin C status in large datasets collected in the United States and Europe.

Their results suggest that certain groups might need more dietary vitamin C than others to achieve the same vitamin C blood concentrations. Age and biological sex were minor factors, but higher body weight, regular smoking habits, blood markers for diabetes mellitus, and high circulating C-reactive protein (also known as CRP, a blood marker of inflammation) were the more influential factors.

For example, their data showed that people who weigh over 220 lbs could need up to three times as much vitamin C as those who weigh half as much. This can be at least partially explained as a dilution effect, as a larger body needs more vitamin C than a smaller one. It is thought that heavy smoking, the presence of diabetes, or high CRP levels can all increase reactive oxygen species in the body, thus explaining an increased need for vitamin C.

Although smoking status is already considered in the RDA for vitamin C set by the National Academy of Medicine, the other factors listed here are not. In all, this information from Dr. Carr suggests a personalized approach to vitamin recommendations might be needed for everyone to achieve optimum vitamin C status. 🌐

References

Carr, Block, and Lykkesfeldt
Nutrients **14** (2022);
doi: 10.3390/nu14071460

Carr and Lykkesfeldt
Nutrients **15** (2023);
doi: 10.3390/nu15071657



DAM PROUD DAY

Oregon State University's annual day of giving!

GET READY

Set a reminder for **April 24**.

GET SET

Choose the Health Aging Research Fund or the Micronutrient Information Center Fund.

GIVE!

Go to **lpi.pub/DamProud** and make a donation!

All donations to the LPI on April 24 will unlock special challenge gifts!

Don't want to give online? No problem.

Any check to the Linus Pauling Institute designated "For Dam Proud Day" will count towards our challenge goals.
Dam Proud Day gifts can be made to any lab or program at the Institute.



Oregon State University
Linus Pauling Institute

LINUS PAULING INSTITUTE
DIGITAL DIGEST

Alexander Michels, Newsletter Editor
Victoria J. Drake, Associate Editor
Sandra Uesugi, Assistant Editor

Oregon State University
307 Linus Pauling Science Center
2900 SW Campus Way
Corvallis, Oregon 97331

phone: 541-737-5075
fax: 541-737-5077
email: lpi@oregonstate.edu
website: lpi.oregonstate.edu