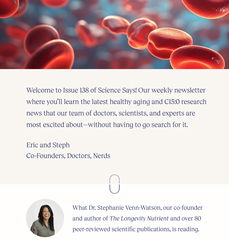
A Simple But Powerful Predictor of Longer Life

June 29, 2025



Welcome to Issue 138 of Science Says! Our weekly newsletter where you'll learn the latest healthy aging and CIS0 research news that our team of doctors, scientists, and experts are most excited about--without having to go search for it.

Eric and Steph
Co-Founders, Doctors, Nerds

What Dr. Stephanie Venn-Watson, our co-founder and author of *The Longevity Nutrient* and over 80 peer-reviewed scientific publications, is reading.

HEALTHY AGING

Let's talk HRR (a biomarker of resilience)

There has been increasing interest in the role of both hemoglobin and red blood cell distribution width (aka RDW) as key biomarkers of long-term health. A recent paper published in *Nature's Scientific Reports* conducted a massive study into just how well hemoglobin, RDW and a combined biomarker called HRR predicted an individual person's healthy lifespan. As well as how, as a population, we're doing on that lifespan front. Let's dive in.

But first, what are hemoglobin, RDW and HRR?

Well, that's a great place to start.

- **Hemoglobin is a protein in red blood cells** that carries and delivers oxygen to our tissue. Hemoglobin is routinely measured during lab checkups, and low hemoglobin levels are used to identify people with anemia. In general, we want to have healthier, higher hemoglobin levels. Unfortunately, as described by Wacka et al., our hemoglobin levels tend to decline as we age.
- **Red blood cell distribution width (RDW)** measures how much variability there is in red blood cell volume and size. People with high RDW have unstable red blood cells. In general, we want to have lower RDW. This is because, as described by Yadav et al., many studies have linked lower RDW to better long-term health. And as you can see in the figure below, those studies have been increasing.
- **The hemoglobin-to-RDW ratio (HRR)** is an emerging predictor of numerous long-term health outcomes. Specifically, higher HRR is good, and lower HRR is bad. Which makes sense, given what you now know about hemoglobin and RDW.

So, to summarize, we typically want higher hemoglobin, lower RDW and higher HRR.

How did this latest study look at potential predictors of longer life?

Lai et al. looked at a cohort of 28,825 participants from the U.S. National Health and Nutrition Examination Survey (1999-2018) to evaluate how well HRR predicted mortality. They used robust statistical models, including:

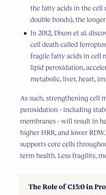
- Weighted Cox regressions
- Restricted cubic spline models
- Subgroup and sensitivity analyses
- Trend tests for temporal trends
- Fully adjusted models controlling for potential confounding factors

By doing so, this study was able to not only determine associations between HRR and mortality, but predicted causality.

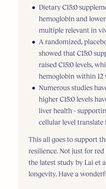
Got it. So, what did they find?

There were two key findings:

First, as expected, higher HRR was linked to lower risks of mortality from any cause, as well as the two leading causes of death: cancer and cardiovascular disease. Specifically, people who had the absolute highest HRR were the healthiest and most protected compared to those who had the lowest HRR.



Second, there was a concerning trend of decreasing HRR in the U.S. population over time. This trend of decreasing HRR coincides with the increase in aging-associated conditions among younger people, especially among those born since the 1990s and are now in their 30s.



The bottom line: The Lai et al. study adds to the growing body of evidence that HRR is an easy-to-measure biomarker of individuals' lifespan potential, and that interventions to protect a higher HRR could support our long-term health - for both individuals and global populations.

But is there an explanation for how higher HRR causes longer life?

Wonderfully, yes.

- As we age, our cell membranes - including our red blood cells - become more fragile. This fragility is due to cells' increased susceptibility to attack by oxygen (aka lipid peroxidation).
- A.J. Hulbert showed that cell membranes with more polyunsaturated fatty acids are more fragile and susceptible to peroxidation due to multiple double bonds in their structure. In fact, he showed that the more stable the fatty acids in the cell membrane (aka the fewer the double bonds), the longer was a species' lifespan.
- In 2012, Dixon et al. discovered an entirely new form of cell death called ferroptosis, which is caused by - yes - fragile fatty acids in cell membranes. The result? Higher lipid peroxidation, accelerated aging, and impaired metabolic, liver, heart, immune and cognitive function.

As such, strengthening cell membranes against lipid peroxidation - including stabilizing red blood cell membranes - will result in healthier, higher hemoglobin, higher HRR, and lower RDW. This protective function also supports core cells throughout our body, translating to long-term health. Less fragility, more stability.

The Role of C15:0 in Protecting Healthy Hemoglobin, RDW and HRR.

As a stable, odd-chain saturated fatty acid, C15:0 is a goldilocks nutrient that strengthens and stabilizes cell membranes, including red blood cells.

- Soboleva et al. showed that children with higher C15:0 concentrations in their red blood cell membranes had healthier, higher hemoglobin, lower lipid peroxidation, and RBCs with longer lifespans.
- Dietary C15:0 supplementation successfully raised hemoglobin and lowered RDW within weeks in multiple relevant in vivo models.
- A randomized, placebo-controlled clinical trial showed that C15:0 supplementation significantly raised C15:0 levels, which resulted in raised hemoglobin within 12 weeks.
- Numerous studies have shown that people with higher C15:0 levels have better metabolic, heart, and liver health - supporting that C15:0's benefits at the cellular level translate into whole body health.

This all goes to support that C15:0 directly supports our resilience. Not just for red blood cells, but as shown in the latest study by Lai et al., our long-term health and longevity. Have a wonderful week, everyone!

Dive deeper into the science

READ THE RELEVANT STUDIES

- Lai et al. Trends in hemoglobin-to-red cell distribution width ratio and its prognostic value for mortality: a nationwide cohort study.
- Wacka et al. Anemia and its connections to inflammation in older adults: a review
- Yadav et al. A systemic review of red blood cells biomarkers in human aging.
- AJ Hulbert. On the importance of fatty acid composition of membranes for aging.
- Dixon et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death.
- Sobolieva et al. Fatty acids of the lipid fraction of erythrocyte membranes and intensity of lipid peroxidation.
- Venn-Watson et al. Efficacy of dietary odd-chain saturated fatty acid pentadecanoic acid parallels broad associated health benefits in humans: could it be essential?
- Venn-Watson et al. Modified fish diet shifted serum metabolome and protected red blood cell health in dolphins: potential role of odd-chain saturated fatty acids.
- Robinson et al. C15:0 Supplementation in Young Adults at Risk for Metabolic Syndrome: A Randomized Controlled Trial.
- Li et al. Saturated Fatty Acid Biomarkers and Metabolic and Heart Health: A Meta-Analysis of Prospective Studies
- Kratz, M. et al. Dairy fat intake is associated with glucose tolerance, hepatic and systemic insulin sensitivity, and liver fat in humans.

- Nerd out on all the C15:0 science at Discover15.com