



*Cognitive Vitality Reports<sup>®</sup> are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.*

## Phosphatidylcholine and Lecithin

### Evidence Summary

No strong evidence to support roles for dementia prevention or anti-aging properties, but they have a good safety profile.

**Neuroprotective Benefit:** RCTs report no substantial benefit in patients with Alzheimer's or Parkinson's and epidemiological evidence is lacking, but reduced phosphatidylcholine levels in plasma may predict cognitive decline.

**Aging and related health concerns:** One study indicated an association of phosphatidylcholine levels and mortality risk, but is confounded because the effect was dependent on the composition of the lipid linked to phosphatidylcholine.

**Safety:** Generally considered safe. One cohort study reports an association with prostate cancer risk, but the association may be related to other aspects of dietary sources of choline.



**What are they?** Phosphatidylcholine is a major type of phospholipid and a primary component of cell membranes (phospholipids are lipids with a phosphate head). Supplements are often derived from egg yolk or soybeans. Phosphatidylcholine is a major component of lecithin, a yellow-brown fatty substance found in egg yolk, organ meats, nuts, and spinach. Although lecithin contains substances other than phosphatidylcholine, the terms are sometimes used interchangeably in medical literature. Phosphatidylcholine supplements are well-absorbed through the gut (e.g. [Zierenberg 1982](#)).

**Neuroprotective Benefit:** RCTs report no substantial benefit in patients with Alzheimer's or Parkinson's and epidemiological evidence is lacking, but reduced phosphatidylcholine levels in plasma may predict cognitive decline.

Types of evidence

- 1 meta-analysis of RCTs with lecithin for treatment but not prevention of cognitive decline
- 1 cohort with internal replication that depletion of some forms predicts risk of dementia
- A handful of observational studies reporting changes in levels with Alzheimer's

Lecithin phosphatidylcholine supplements, or krill oil, have failed to successfully treat Alzheimer's or cognitive aging with lecithin, in the majority of RCTs, although one or two trials reported some minimal effect. For example, a 2003 Cochrane meta-analysis reported on 10 trials in Alzheimer's patients, 1 trial in Parkinson's, and 1 trial in patients with subjective memory impairment. While no benefits were reported in the Alzheimer's or Parkinson's patients, some benefits were reported in patients with subjective memory impairment, however the effects of this single trial have not been replicated ([Higgins 2003](#)).

It should be noted that all of these trials were for short-term supplementation, and longer treatment may be necessary for benefit. The long-term intake of phosphatidylcholine, whether via diet or supplements, has not been associated with altered risk for cognitive decline in any epidemiological study to date. However, a handful of observational studies report changes in levels with Alzheimer's. Low levels of some phosphatidylcholine lipids was a major component of a blood-based lipidomic biomarker panel reported to predict conversion from mild cognitive impairment to full Alzheimer's disease within 2-3 years ([Mapstone 2014](#)). The authors speculate that the phosphatidylcholine levels indicate cell membrane integrity.



There are several possible mechanisms by which phosphatidylserine could potentially benefit the brain. Treatment can raise choline levels, providing a precursor for the synthesis of acetylcholine, a neurotransmitter lost early in Alzheimer's disease (and also the target of most FDA-approved drugs for Alzheimer's). Phosphatidylcholine is also a major component of cell membranes and critical for some types of intracellular signaling.

**ApoE4 interactions:** Uncertain. Apolipoprotein E binds to phospholipids (e.g. phosphatidylcholine) and this binding is slightly altered with E4. However, this binding should not affect the primary suggested mechanisms of action of phosphatidylcholine, of providing a source of choline for acetylcholine synthesis and a source of phosphatidylcholine for cell membrane integrity.

**Aging and related health concerns:** One study indicated an association of phosphatidylcholine levels and mortality risk, but is confounded because the effect was dependent on the composition of the lipid linked to phosphatidylcholine.

#### Types of evidence

- 1 cohort reporting that blood levels associate with mortality risk, although direction of association (increase vs decrease) depends on the type of lipid in the phosphatidylcholine

There are no studies indicating that phosphatidylcholine supplementation could protect against age-related changes in function, mortality risk, or cell membrane integrity. Phosphatidylcholine levels in the blood were associated with mortality risk in a 2014 cohort publication but the direction of the association depended heavily on the type of lipid linked to the phosphatidylcholine. Saturated and monounsaturated phosphatidylcholine were associated with a *higher* risk of mortality, while long-chain polyunsaturated fatty acids (omega-3 or omega-6) were associated with *less* risk of mortality. Combining the 6 lipids with the most protective association and the 6 lipids with the most harmful association predicted a 3x increased risk of mortality. These effects might be related to diet and exercise. For example, fish oil supplementation and possibly exercise can increase the percentage of phospholipids that contain polyunsaturated fatty acids ([Sigruener 2014](#)).

*Stroke:* Treatments to increase choline supply have been examined as an acute treatment for stroke, but the evidence has focused on citicoline rather than phosphatidylcholine and lecithin.



**Safety:** Generally considered safe. One cohort study reports a substantial association with prostate cancer risk, but the association is may be related to other aspects of dietary sources of choline.

*Prostate cancer:* High dietary intake of choline (primarily lecithin) was associated with a 70% higher risk of lethal prostate cancer (Hazard ratio (HR): 1.7, 95% CI 1.18 to 2.45) although this association could be due to other components of typical dietary sources of choline (meat, milk, and eggs) ([Richman 2012](#)).

*Cardiovascular risk:* Choline levels in blood and plasma have been linked to a higher risk of major cardiac events ([Danne 2007](#)). Similar to the prostate cancer study, it is unclear whether this is due to other components of typical dietary sources of choline. It is also unclear whether different phosphatidylcholine lipids will have a different relationship, as they do for mortality risk. Phosphatidylcholine in the gut can also increase trimethylamine-N-oxide (TMAO levels), which could, in theory, worsen atherosclerosis ([Ussher 2013](#)).

#### **Dosing and Sources:**

- **Phosphatidylcholine supplements.** Supplements can vary in their lipid content. Based on the mortality association study ([Sigruener 2014](#)), supplements high in polyunsaturated fatty acids (either omega-3 or omega-6) might be beneficial while supplements high in saturated or monounsaturated lipids might be harmful. However, the ratios of these different lipids may be altered substantially by metabolism and exercise as well as dietary intake. Supplements taken orally in clinical trials range in dose from 350 mg to 6 g per day, but a therapeutic dose for brain health has not been established.
- **Lecithin:** Doses in randomized trials have ranged from 1 to 50 grams daily, generally with no major side effects reported. Lecithin is the major dietary source of phosphatidylcholine. It is a yellow-brown fatty substance found in egg yolk, organ meats, nuts, and spinach.
- **Citicoline** (CDP-choline) is a related treatment. It can raise choline levels in the body and brain for the synthesis of acetylcholine and phosphatidylcholine (e.g. [Conant 2004](#)).

**Future research:** More research on the types of supplementation that alters age-related health and biomarkers, including phosphatidylcholine lipid species in the blood, is needed. No randomized trials on lecithin or phosphatidylcholine in relation to age-related health or cognition are reported as ongoing in ClinicalTrials.gov.



**Search terms:**

- Pubmed - "phosphatidylcholine" with filter for meta-analysis & Systematic review, "phosphatidylcholine, mortality" with filter of clinical trial or meta-analysis or systematic review, "phosphatidylcholine, aging, supplement," "phosphatidylcholine, aging (or mortality), cohort," "phosphatidylcholine, telomere," "lecithin, stroke", "lecithin, cognitive", "lecithin, brain"
- www.Phosphatidylcholine.org (claims with no references)

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