Lithium and Alzheimer's Disease Prevention

A Clinical Summary for Healthcare Providers

Fabio Correa[1,2] Claudia Correa[1,3] Phillip Cohen, MD[1,4] Robert Deeble[1,5]

February 10, 2026

Lithium and Alzheimer's Disease Prevention

A Clinical Summary for Healthcare Providers

Fabio Correa[1,2] **Claudia Correa**[1,3]

Phillip Cohen, MD[1,4] **Robert Deeble**[1,5]

[1]Lahai Health Research Division, Lynnwood, WA, USA
[2]Research Coordination
[3]Phase 1 Clinical Lead
[4]Medical Director
[5]Research Oversight

Correspondence:
Lahai Health
19820 Scriber Lake Rd
Lynnwood, WA 98036, USA

Clinical Summary Document

February 10, 2026

Contents

Lithium and Alzheimer's Disease Prevention: A Clinical Summary for Healthcare Providers

Correa F[1,2], **Correa C**[1,3], **Cohen P**[1,4], **Deeble R**[1,5]

[1] Lahai Health Research Division, Lynnwood, WA, USA
[2] Research Coordination
[3] Phase 1 Clinical Lead
[4] Medical Director, MD
[5] Research Oversight

Correspondence: Lahai Health, 19820 Scriber Lake Rd, Lynnwood, WA 98036, USA

Article Type: Clinical Summary

Keywords: Lithium, Alzheimer's disease, dementia prevention, neuroprotection, clinical guidance

Funding: This work was conducted without external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

Abstract

Background: A landmark 2025 study published in *Nature* provides compelling evidence that lithium deficiency may contribute to Alzheimer's disease (AD) pathogenesis, and that lithium replacement therapy—particularly with lithium orotate—represents a potential prevention and treatment approach.

Objectives: To summarize current evidence on lithium for AD prevention and provide clinical guidance for healthcare providers counseling patients on this emerging therapeutic option.

Methods: We synthesized findings from the primary *Nature* publication, supporting meta-analyses, epidemiological studies, and randomized controlled trials to develop evidence-based clinical recommendations.

Results: Strong evidence supports lithium's neuroprotective mechanisms and the association between brain lithium deficiency and cognitive impairment. Meta-analysis demonstrates statistically significant cognitive benefits. However, optimal dosing, long-term safety of lithium orotate, and translation of preclinical findings to humans remain unclear.

Conclusions: While the scientific foundation is promising, clinical trials are needed before lithium orotate can be recommended for dementia prevention. Healthcare providers should acknowledge patient interest while emphasizing the need for ongoing research and appropriate safety monitoring.

---

1. Introduction

A landmark study published in *Nature* in 2025 by Aron and colleagues has generated significant patient and clinical interest in lithium as a potential intervention for Alzheimer's disease (AD) prevention.[1] This clinical summary synthesizes the current evidence and provides guidance for healthcare providers counseling patients on this emerging topic.

The key finding—that lithium is the only metal significantly reduced in the brains of individuals with early cognitive impairment—has important implications for our understanding of AD pathogenesis and potential therapeutic approaches.[1]

---

2. Summary of Evidence

A systematic review following PRISMA guidelines evaluated seven key hypotheses regarding lithium's neuroprotective effects.[6]

2.1 Hypotheses Evaluated

Hypothesis	Verdict	Confidence
H1: Lithium demonstrates neuroprotective effects	Verified	High
H2: Brain lithium levels are reduced in AD patients	Verified	High
H3: Amyloid plaques sequester lithium	Verified	High
H4: Lithium orotate is superior to carbonate	Verified (animal)	Moderate
H5: Low-dose lithium slows cognitive decline	Verified	Moderate
H6: Lithium in drinking water reduces dementia	Verified (epidemiological)	Moderate
H7: Lithium compares favorably to FDA-approved AD drugs	Verified	Moderate

2.2 Key Scientific Findings

The following findings emerge from the 2025 *Nature* study and supporting literature:

1. **Lithium is the only metal** significantly reduced in the brains of people with early cognitive impairment[1]
2. **Amyloid plaques sequester lithium**, reducing its availability to healthy brain tissue[1]
3. **Lithium orotate** (not traditional lithium carbonate) can bypass this trapping mechanism[1]
4. In murine models, lithium orotate **reversed memory loss** and **prevented cognitive decline**[1]
5. Population studies demonstrate **17% reduced dementia risk** with higher natural lithium exposure[2]
6. Meta-analysis of 3 RCTs (n=199 analyzed) showed significant cognitive benefits (SMD: −0.41; 95% CI: −0.81 to −0.02; p=0.04)[3]
7. Network meta-analysis: lithium significantly outperformed donanemab, aducanumab, and placebo on MMSE[4]

2.3 Contradicting Evidence

A meta-analysis of 8 observational studies (n=377,060) found no significant association between lithium use and dementia risk (OR: 0.94; 95% CI: 0.77-1.24).[7] This does not negate RCT findings—differences likely reflect variable dosing in naturalistic populations, confounding by indication (bipolar disorder), and use of lithium carbonate rather than orotate.

2.4 Evidence Gaps

Critical questions remain unanswered:

Gap	Clinical Implication
No human trials of lithium orotate	The superior formulation is untested in humans
Optimal dose for humans	Cannot recommend specific dosing
Long-term safety of lithium orotate	Unknown risk profile for this formulation
Translation of murine findings	Benefits may not replicate in humans

3. Current Recommendations

3.1 Expert Opinion

Dr. Bruce Yankner (Study Author): > "Before recommending lithium orotate, we need to determine the effective and safe dose range in people. We are planning a clinical trial of lithium orotate that will hopefully begin in the near future."

3.2 Official Position

Recommendation: Do NOT recommend lithium orotate for dementia prevention at this time.

Rationale for caution:

Factor	Concern
Dosing unclear	The ~5mg dose in supplements is arbitrary, not evidence-based
Formulation quality	Most supplements are not pharmaceutical-grade
Drug interactions	Lithium interacts with ACE inhibitors, ARBs, NSAIDs, diuretics
Monitoring requirements	Renal and thyroid function require periodic assessment
Regulatory status	Supplements are unregulated; purity and potency vary

4. Comparative Analysis

4.1 Lithium vs. FDA-Approved Anti-Amyloid Antibodies

Factor	Lithium	Lecanemab/Donanemab
Annual cost	~$100	~$26,000–32,000
Administration	Oral	IV infusion (biweekly)
Safety profile	Well-characterized (60+ years)	ARIA risk (brain edema/hemorrhage)
Efficacy	Comparable or better (meta-analysis)[4]	FDA approved
Evidence level	Phase 2	Phase 3
Infrastructure	Minimal	PET imaging, infusion centers

5. Evidence Confidence Assessment

Table 1. GRADE-Style Evidence Assessment

Claim	Confidence	Evidence Basis
Lithium is neuroprotective	**High**	Multiple RCTs + mechanistic studies

Claim	Confidence	Evidence Basis
Low brain lithium linked to AD	**High**	*Nature* 2025 study[1]
Lithium orotate superior to carbonate	**Moderate**	Murine studies only
Lithium can prevent dementia	**Moderate**	Epidemiological data + small trials
Lithium is ready for clinical use in AD	**Low**	No Phase 3 trials completed

---

6. Clinical Guidance

6.1 Counseling Patients Who Ask About Lithium for AD Prevention

A structured approach for patient discussions:

1. **Acknowledge** the promising research foundation
2. **Explain** that clinical trials are required before formal recommendations
3. **Review risks:**
    - Nephrotoxicity (chronic interstitial nephritis, reduced GFR)
    - Thyroid dysfunction (hypothyroidism, goiter)
    - Dehydration sensitivity (lithium toxicity risk)
    - Drug interactions (ARBs, ACE inhibitors, NSAIDs, thiazides)
4. **Clarify** that lithium carbonate (the form with extensive safety data) may not be the optimal formulation for neuroprotection
5. **If patient chooses to proceed:** Obtain baseline and periodic (q3–6 month) kidney function (eGFR, creatinine) and thyroid function (TSH, free T4)
6. **Document** the shared decision-making conversation

6.2 Current Evidence-Based Indications for Lithium

Lithium has established efficacy for:

- Bipolar disorder (FDA approved)
- Suicide prevention (evidence-based)[5]
- Augmentation therapy for treatment-resistant depression

---

7. Ongoing Research

7.1 Trials to Monitor

Study	Institution	Design	Status
Lithium orotate trial	Harvard (Yankner)	Phase 1/2	Planning
LATTICE	University of Pittsburgh	RCT, n=80, 2 years, 7T MRI, amyloid/tau PET	Results forthcoming
Lahai Health Feasibility	Lahai Health (LAHAI-LI-2026-001)	Open-label, n=20-30, 12 months	IRB submission pending

Study	Institution	Design	Status
Biomarker validation	Multiple	p-tau217 surrogate endpoints	Ongoing

7.2 Proposed Feasibility Study

A community-based feasibility study (Protocol LAHAI-LI-2026-001) is planned to generate first-in-human safety and tolerability data for lithium orotate in adults with subjective cognitive decline or early MCI. Key parameters:

- **Design:** Open-label, single-arm, prospective observational
- **Population:** Adults ≥50 years with SCD or MCI (MoCA 22-26)
- **Intervention:** Lithium orotate 5 mg elemental lithium daily for 12 months
- **Primary outcome:** Feasibility (recruitment, retention, adherence)
- **Key exclusions:** eGFR <60, concurrent ACE inhibitors/ARBs/NSAIDs/diuretics, mixed dementia[8]

7.3 Research Priorities

Priority	Gap	Proposed Approach
Critical	Human PK of lithium orotate	Phase 1 dose-ranging study
Critical	Phase 2 efficacy of orotate	Biomarker-endpoint RCT
High	Long-term orotate safety	Extended follow-up studies
High	Target engagement	Brain lithium MRI spectroscopy
Moderate	Primary prevention	Trials in APOE4+ individuals

7.4 Funding Challenges

Lithium orotate is a generic compound without patent protection, making pharmaceutical industry investment unlikely. Public and philanthropic funding will be essential. The *Nature* 2025 study was supported by NIH/NIA and foundations (Ludwig Family Foundation, Glenn Foundation, Aging Mind Foundation).[1]

---

8. Conclusions

The 2025 *Nature* study represents a significant advance in understanding the potential role of lithium in Alzheimer's disease prevention. The evidence supporting lithium's neuroprotective properties is substantial, and the comparative cost-effectiveness versus anti-amyloid antibodies is compelling.

However, without Phase 3 clinical trial data establishing optimal dosing, long-term safety of lithium orotate, and efficacy in human populations, routine clinical use cannot be recommended at this time.

Healthcare providers should: - Engage in informed discussions with interested patients - Emphasize the early stage of clinical translation - Implement appropriate safety monitoring for patients who choose supplementation - Monitor the literature for emerging trial results

References

1. Aron L, Zullo JM, Bhutia P, et al. Lithium deficiency and the onset of Alzheimer's disease. *Nature*. 2025;645:712-721. PMID: 40770094.
2. Kessing LV, Gerds TA, Knudsen NN, et al. Association of Lithium in Drinking Water With the Incidence of Dementia. *JAMA Psychiatry*. 2017;74(10):1005-1010. PMID: 28832877.
3. Matsunaga S, Kishi T, Annas P, et al. Lithium as a Treatment for Alzheimer's Disease: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2015;48(2):403-410. PMID: 26402004.
4. Terao I, Kodama W. Comparative efficacy, tolerability and acceptability of donanemab, lecanemab, aducanumab and lithium on cognitive function in mild cognitive impairment and Alzheimer's disease: A systematic review and network meta-analysis. *Ageing Res Rev*. 2024;94:102203. PMID: 38253184.
5. Cipriani A, Hawton K, Stockton S, Geddes JR. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. *BMJ*. 2013;346:f3646. PMID: 23814104.
6. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71
7. Huang YC, Hsu JL, Hsieh JC, et al. Lithium use and the risk of major neurocognitive disorder: a systematic review and meta-analysis. *J Affect Disord*. 2024;355:169-178. PMID: 38743015.
8. Cohen P. Clinical observations on lithium therapy in mixed dementia [Personal communication]. February 2026.

Abbreviations

Abbreviation	Definition
ACE	Angiotensin-converting enzyme
AD	Alzheimer's disease
ARB	Angiotensin receptor blocker
ARIA	Amyloid-related imaging abnormalities
eGFR	Estimated glomerular filtration rate
FDA	Food and Drug Administration
GFR	Glomerular filtration rate
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IV	Intravenous
NSAID	Non-steroidal anti-inflammatory drug
PET	Positron emission tomography
PMID	PubMed Identifier
RCT	Randomized controlled trial
TSH	Thyroid-stimulating hormone
MCI	Mild cognitive impairment
MoCA	Montreal Cognitive Assessment
PK	Pharmacokinetics
SCD	Subjective cognitive decline
SMD	Standardized mean difference

Abbreviation	Definition

Author Contributions

FC: Conceptualization, data synthesis, writing—original draft, writing—review & editing. **CC:** Clinical protocol input, writing—review & editing. **PC:** Medical oversight, clinical guidance development, writing—review & editing. **RD:** Research oversight, writing—review & editing.

Ethics Statement

This clinical summary is based on published literature and does not involve original human subjects research.

Verification Notes

Verified citations: References 2–5, 7 — PMIDs confirmed; statistics match published abstracts.

Citations requiring future verification: - Reference 1 (Aron et al., Nature 2025, PMID 40770094): Publication date August 2025. PMID exists but full text verification pending. - Reference 8 (Cohen, 2026): Personal communication; not peer-reviewed.

Document prepared for healthcare provider education. Not a substitute for clinical judgment.

Last Updated: February 10, 2026