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LITHIUM AND ALZHEIMER'S DISEASE: POTENTIAL NEUROPROTECTIVE EFFECTS AND THERAPEUTIC PERSPECTIVES

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ABSTRACT

Lithium is an established mood stabilizer whose possible use in Alzheimer's disease (AD) has emerged from convergent molecular, animal, observational, and early clinical evidence. The principal rationale is that lithium may act on several processes implicated in AD rather than on a single lesion: glycogen synthase kinase-3β (GSK-3β) signaling, tau phosphorylation, amyloid precursor protein processing, neuroinflammation, oxidative and mitochondrial stress, autophagy, neurogenesis, and synaptic plasticity. Animal studies generally report preserved memory and reduced amyloid-related pathology, while small human studies suggest that subtherapeutic lithium may attenuate cognitive decline or modify cerebrospinal-fluid biomarkers. Observational cohorts also associate lithium exposure with lower dementia incidence, but these findings are vulnerable to confounding by indication, comorbidity, treatment adherence, and healthcare use. Evidence is not uniformly positive: a Scottish cohort exposed to extremely low environmental lithium did not support dementia protection, and a recent randomized feasibility trial in mild cognitive impairment found no significant effect on any of six prespecified coprimary outcomes, although one memory measure declined more slowly with lithium. The therapeutic challenge is therefore not simply whether lithium is neuroprotective, but which patients, dose, formulation, exposure duration, and biomarker-defined disease stage are most likely to benefit. Lithium remains an investigational strategy for AD prevention or treatment, not a substitute for established clinical care.

KEYWORDS

Lithium, Alzheimer's Disease, Treatment

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Introduction

Alzheimer's disease is biologically heterogeneous. Amyloid-β (Aβ) plaques and neurofibrillary tangles containing hyperphosphorylated tau remain defining pathological features, but cognitive decline also reflects synaptic dysfunction, neuroinflammation, impaired energy metabolism, oxidative stress, defective proteostasis, and neuronal loss. Aβ oligomers can disturb synaptic function, mitochondrial activity, calcium homeostasis, and redox balance, whereas activated glia can be protective through Aβ clearance or harmful through cytokine, reactive oxygen, and synaptic-loss pathways (Carrillo-Mora et al., 2014; Novoa et al., 2022). This complexity creates a rationale for repurposing drugs with pleiotropic actions.

Lithium is attractive because it is inexpensive, orally available, and supported by decades of clinical experience in bipolar disorder. Its proposed relevance to AD is centered on inhibition of GSK-3, particularly GSK-3β, a kinase implicated in tau phosphorylation and amyloidogenic processing. Lithium can inhibit GSK3α and GSK3β directly, but in vivo it also affects GSK3 through signaling networks involving Akt and β-arrestin 2 (Freland & Beaulieu, 2012). The AD hypothesis is consequently broader than "lithium lowers tau": lithium may influence several interacting pathways that determine neuronal resilience.

This review evaluates the evidence in four layers: molecular and cellular mechanisms; primary animal studies; human observational and randomized evidence; and practical therapeutic perspectives. The central distinction is between biological plausibility and clinical efficacy. The former is substantial; the latter remains preliminary and mixed.

Molecular and Cellular Basis of Potential Neuroprotection

GSK-3β, tau, and amyloid processing

GSK-3β is a plausible convergence point between lithium pharmacology and AD biology. GSK-3β is a major tau kinase, and its dysregulation can promote excessive tau phosphorylation. GSK3 activity also affects amyloid precursor protein cleavage and Aβ formation; reviews of the pathway describe overactive GSK3 as a contributor to tau pathology, amyloid production, neuroinflammation, and oxidative damage (Zhao et al., 2024). Inhibition of GSK3 may therefore reduce both cytoskeletal disruption from hyperphosphorylated tau and upstream amyloidogenic signaling.

This mechanism should not be interpreted as proof that GSK-3β is a sufficient therapeutic target. GSK3 has many substrates and participates in development, metabolism, cytoskeletal regulation, and cell survival. Broad or excessive inhibition could produce unintended effects. Lithium is also not a highly selective GSK-3β inhibitor: its actions depend on concentration, intracellular context, ion competition, and signaling networks. The mechanistic advantage of lithium may therefore be distributed pathway modulation rather than target-specific blockade. A review of lithium pharmacology identifies GSK3 inhibition, homeostatic synaptic plasticity, and microRNA regulation as interrelated mechanisms, while also emphasizing that the precise translation from molecular action to clinical benefit remains unresolved (A et al., 2024).

Amyloid-β, BACE1, and proteostasis

The amyloid hypothesis has become more nuanced because soluble Aβ oligomers may be more closely related to synaptic dysfunction than insoluble plaques. This distinction matters for lithium: reductions in plaque burden alone would not establish that lithium prevents the toxic species most relevant to cognition. Nevertheless, lithium has shown effects at several points in amyloid biology. In a primary rat study, Wilson et al. tested the microdose formulation NP03 and reported GSK-3β inactivation, lower BACE1 expression and activity, reduced amyloid levels, rescued memory loss, and improved hippocampal neurogenesis (Wilson et al., 2017). The finding links lithium exposure to both amyloid processing and functional outcomes, but it remains a preclinical result in a model of progressive amyloid pathology.

Lithium has also been proposed to enhance autophagy and protein-clearance pathways. The 2024 mechanistic review by Shen et al. summarizes preclinical evidence for increased autophagy, reduced amyloid deposition, reduced tau phosphorylation, preservation of mitochondrial function, and suppression of apoptosis, oxidative stress, and neuroinflammation (Shen et al., 2024). These effects are biologically coherent, but the review-level synthesis combines different lithium salts, doses, species, disease models, and outcome definitions. It should therefore generate hypotheses rather than be treated as a single replicated clinical effect.

Neuroinflammation and neuron–glia homeostasis

Neuroinflammation is neither uniformly harmful nor uniformly beneficial. Microglia and astrocytes can clear Aβ and support tissue repair, but sustained activation can release tumor necrosis factor-α, interleukin-1β, reactive oxygen species, and reactive nitrogen species, thereby promoting synaptic loss and neuronal injury (Novoa et al., 2022). A treatment that merely suppresses glial activity could therefore be detrimental if it also blocks protective clearance.

Lithium may instead modify the balance of neuron–glia signaling. In a primary proteomic and gene-ontology study of triple-transgenic AD mice, Rocha et al. found treatment-related changes in hippocampal neuronal–glial interaction networks, including pathways involving membrane protein localization, oligodendrocyte differentiation, myelin sheath, protein synthesis, DNA repair, and cellular homeostasis (Rocha et al., 2020). These results support a systems-level neuroprotective response, but they do not identify which molecular change is necessary for preserved cognition or whether the same response occurs in human AD.

Lithium's immunomodulatory effects may also be relevant outside the brain. A clinical and translational review describes lithium as immunomodulatory and neuroprotective, while noting that its dementia and AD findings are favorable but still limited compared with its established psychiatric indications (Rybakowski, 2022). The appropriate interpretation is that inflammation is a plausible mediator, not that lithium has an established anti-inflammatory treatment effect in AD patients.

Oxidative stress, mitochondria, neurotrophic signaling, and synapses

Oxidative stress and mitochondrial dysfunction amplify Aβ- and tau-associated injury. AD-related oxidative damage can impair energy production, membrane integrity, calcium handling, and synaptic transmission. Lithium's proposed effects include preservation of mitochondrial function, antioxidant signaling, and reduced apoptosis (Shen et al., 2024). These claims are primarily supported by cellular and animal studies; direct clinical confirmation using validated redox or mitochondrial biomarkers is limited in the evidence reviewed here.

Neurotrophic and synaptic mechanisms may be especially important because synaptic failure is a proximate link between pathology and memory impairment. BDNF supports neuronal survival and synaptic plasticity, and lower BDNF signaling has been associated with Aβ accumulation, tau phosphorylation, neuroinflammation, and apoptosis (Gao et al., 2022). In the APP transgenic mouse study by Nunes et al., chronic microdose lithium preserved memory, reduced senile plaques, prevented cortical and hippocampal neuronal loss, and increased cortical BDNF density relative to untreated transgenic mice (Nunes et al., 2015). The study supports a coordinated neurotrophic effect, but it cannot establish whether BDNF is a causal mediator or a downstream correlate.

Lithium may also improve plasticity through CREB-related transcriptional pathways. The NP03 rat study reported restoration of impaired binding of CRTC1 at promoters of synaptic-plasticity genes, together with recovery of memory and neurogenesis (Wilson et al., 2017). These observations provide a bridge between molecular signaling and behavioral performance, yet the model was treated before advanced neurodegeneration and may be more informative for prevention or early intervention than for established dementia.

Evidence from Animal Models

Preclinical evidence is directionally encouraging but heterogeneous. Nunes et al. used APP transgenic mice and administered lithium carbonate at 0.25 mg/kg/day for 8 or 16 months, beginning before or after the appearance of symptoms. Lithium-treated transgenic groups did not show the memory disruption observed in untreated transgenic mice; early treatment was also associated with fewer senile plaques, no neuronal loss in cortex or hippocampus, and greater cortical BDNF density (Nunes et al., 2015). The long exposure and prevention-oriented design are strengths for testing disease modification, but the dose and pharmacokinetics cannot be assumed to correspond to human serum concentrations.

Wilson et al. tested NP03, a microdose formulation, in a rat model with progressive AD-like amyloid pathology. The study reported effects on GSK-3β, BACE1, amyloid levels, memory, synaptic-plasticity gene regulation, and hippocampal neurogenesis (Wilson et al., 2017). This multi-endpoint pattern is stronger than a single histological finding, but it also increases the number of possible pathways and outcome comparisons. Replication across independent models, blinded behavioral testing, dose–exposure measurements, and validation in tau-predominant models are needed before the formulation can be considered disease-modifying.

Rocha et al. provide a complementary systems-biology perspective. Their triple-transgenic mouse study did not primarily establish a behavioral treatment effect; rather, it identified altered neuron–glia interaction networks and homeostatic pathways after prolonged lithium exposure (Rocha et al., 2020). This is useful for mechanism discovery, but proteomic pathway enrichment is not equivalent to clinical efficacy. Across these animal studies, the most consistent themes are preserved memory, reduced amyloid-related pathology, improved neurotrophic or synaptic signaling, and altered cellular homeostasis. The main limitations are model dependence, variable dosing, long treatment periods, and the frequent use of treatment before irreversible neuronal loss.

Human Observational and Clinical Evidence

Observational associations with dementia

Observational findings support a possible preventive effect but do not prove causality. In a US claims-based cohort of adults aged 50 years and older with bipolar disorder, Gerhard et al. found that lithium exposure on 301–365 days of the preceding year was associated with lower dementia risk than non-use (HR 0.77, 95% CI 0.60–0.99). Shorter exposure categories were not associated with lower risk, and anticonvulsant mood stabilizers did not show the same pattern (Gerhard et al., 2015). The exposure-duration gradient and negative-control comparison are helpful, but residual confounding remains possible. Continuous lithium use may identify patients with better treatment engagement, fewer destabilizing episodes, or different healthcare trajectories.

Chen et al. analyzed 29,618 patients from UK secondary mental-health records, including 548 lithium-exposed individuals. After adjustment for sociodemographic variables, smoking, medications, mental-health conditions, and physical comorbidities, lithium use was associated with lower risk of all-cause dementia (HR 0.56, 95% CI 0.40–0.78), AD (HR 0.55, 95% CI 0.37–0.82), and vascular dementia (HR 0.36, 95% CI 0.19–0.69) (Chen et al., 2022). The inclusion of dementia subtypes and extensive covariate adjustment strengthens the association, but the small exposed group and the difficulty of separating bipolar disorder from lithium indication limit generalization to people without psychiatric illness.

Environmental lithium studies are less consistent. A 2024 systematic review identified five studies of trace lithium in drinking water and reported lower dementia incidence or mortality at some concentrations as low as 0.002 mg/L and 0.056 mg/L, while acknowledging uncertainty about the optimal dose (Fraiha-Pegado et al., 2024). In contrast, Duthie et al.'s Scottish cohort of 37,597 people found no evidence that extremely low lithium concentrations protected against later dementia; among women, several low-to-intermediate exposure categories were associated with higher rather than lower risk, while no association was found in men (Duthie et al., 2023). These results may reflect exposure misclassification, ecological measurement, nonlinear effects, sex differences, or chance. They also show why environmental associations cannot be translated directly into a recommended supplement dose.

Randomized and controlled studies

The strongest early clinical evidence comes from MCI rather than established AD. In a 12-month double-blind trial, Forlenza et al. randomized 45 people with aMCI to lithium targeted to 0.25–0.5 mmol/L or placebo. Lithium was associated with lower CSF phosphorylated tau, better performance on the cognitive subscale of the Alzheimer's Disease Assessment Scale, and better attention performance; tolerability was described as good and adherence was 91% (Forlenza et al., 2011). The small sample and short duration limit inference about dementia prevention, but the combination of a clinical measure and a disease-related biomarker is mechanistically informative.

A larger follow-up report from the same research program randomized 61 physically healthy older adults with aMCI to lithium or placebo for two years, followed by an additional 24 months with single-blind follow-up. Lithium was prescribed to 0.25–0.5 mEq/L. The placebo group showed cognitive and functional decline, whereas the lithium group remained stable over two years; lithium-treated participants also performed better on memory and attention tests after 24 months, and CSF Aβ1–42 increased after 36 months (Forlenza et al., 2019). These results are compatible with disease modification, but the sample remains small, and the biomarker changes do not by themselves establish reduced conversion to AD dementia.

Longer-term follow-up is suggestive but must be interpreted cautiously. Damiano et al. recontacted 36 of the original 61 participants 11–15 years later; 30.5% of the recalled sample had died, and psychometric data were available only for surviving participants able to complete testing. The previously lithium-treated group had higher mean MMSE and phonemic verbal-fluency scores than the comparison group (Damiano et al., 2022). Attrition, survival bias, small numbers, and the cross-sectional reassessment make this hypothesis-generating rather than confirmatory evidence.

A newer randomized feasibility trial provides an important counterweight. Gildengers et al. randomized older adults with MCI to two years of low-dose lithium or placebo; 80 participants started treatment. None of six prespecified coprimary outcomes—three cognitive or cognitive-composite measures, hippocampal volume, cortical gray-matter volume, and BDNF—met the prespecified significance threshold. Delayed verbal recall declined by 1.42 points per year in the placebo group and 0.73 points per year in the lithium group, a between-

group difference of 0.69 points per year with P = .05, but the study was framed as a feasibility trial and this isolated result should not be treated as definitive efficacy. Serious adverse events occurred in 29% of lithium participants and 23% of placebo participants; increased creatinine, diarrhea, tiredness, and tremor were among the reported adverse events (Gildengers et al., 2026).

The recent randomized evidence therefore has a mixed profile: earlier small trials suggest cognitive and biomarker benefit, while the newer feasibility RCT did not meet its coprimary efficacy threshold. This discrepancy does not necessarily refute lithium's biological activity. The studies differed in sample, duration, biomarker strategy, lithium exposure, statistical thresholds, and possibly the proportion of participants with amyloid-positive disease. It does mean that routine lithium treatment for MCI or AD cannot be justified on current efficacy evidence.

Dose, Formulation, and Safety Considerations

Lithium's therapeutic window is narrow. Manchia et al. note that conventional psychiatric treatment generally targets serum concentrations above 0.6 mEq/L, although the evidence for that threshold is less definitive than often assumed and lower concentrations may produce molecular or neuroprotective effects (Manchia et al., 2024). The distinction between psychiatric-dose lithium, subtherapeutic lithium, microdose lithium, and trace environmental exposure is therefore essential. These categories cannot be treated as interchangeable because administered dose, serum concentration, brain exposure, treatment duration, and patient susceptibility differ.

Low-dose strategies are attractive because they might preserve pathway effects while reducing toxicity. A systematic review of 18 adult interventional studies defined low-dose lithium approximately as serum levels ≤0.6 mmol/L and found signals of benefit for attenuating cognitive decline, with low-dose lithium generally reported as safe. However, the authors emphasized the small and heterogeneous evidence base (Strawbridge et al., 2022). The review supports feasibility, not a settled risk–benefit ratio for older people with AD.

Safety remains a central design issue. Common lithium effects include nausea, polyuria, tremor, weight gain, and cognitive dulling; lithium can also affect renal, thyroid, and parathyroid function, with rare severe renal insufficiency during long-term use (M & M., 2024). Older adults may be particularly vulnerable because renal function, hydration, sodium balance, polypharmacy, and susceptibility to neurological adverse effects change with age. In the newer MCI trial, creatinine increases, fatigue, diarrhea, and tremor were frequent enough to matter even though no serious adverse event was judged definitely treatment-related (Gildengers et al., 2026). Any future trial must therefore prespecify renal, thyroid, calcium, neurological, cardiovascular, and drug-interaction monitoring rather than treat safety as a secondary issue.

Formulation may be as important as dose. NP03 was developed to deliver microdose lithium to the brain while avoiding the adverse-effect profile associated with conventional formulations; in a rat model it produced effects on GSK-3β, BACE1, amyloid, memory, and neurogenesis (Wilson et al., 2017). Nanolithium reviews describe formulations using much lower nominal doses than classical lithium and identify GSK-3β inhibition as the principal proposed mechanism, but these approaches remain translational and require independent clinical confirmation (Guilliot et al., 2024). A formulation should not be considered safer merely because its nominal dose is lower: brain exposure, systemic exposure, manufacturing consistency, and long-term toxicity must be measured directly.

Methodological Comparison

Study	Design and population	Lithium exposure or comparison	Main outcome	Interpretation and principal limitation
Nunes et al. (2015)	Primary APP-transgenic mouse study	0.25 mg/kg/day; treatment for 8 or 16 months versus water	Memory preserved; early treatment reduced plaques, neuronal loss, and increased cortical BDNF (Nunes et al., 2015)	Strong prevention-oriented preclinical signal; human dose equivalence and model validity remain uncertain
Wilson et al. (2017)	Primary rat model of progressive amyloid pathology	Microdose NP03 versus control	GSK-3β and BACE1 inhibition, lower amyloid, rescued memory, improved neurogenesis (Wilson et al., 2017)	Links target engagement to function; requires replication and testing beyond amyloid-dominant models
Forlenza et al. (2014)	Double-blind randomized trial; 45 people with aMCI; 12 months	Lithium 0.25–0.5 mmol/L versus placebo	Lower CSF P-tau and better ADAS-Cog and attention performance (Forlenza et al., 2011)	Clinical and biomarker signal; small sample and short duration
Forlenza et al. (2019)	Randomized trial; 61 older adults with aMCI; 2-year double-blind phase plus follow-up	Lithium 0.25–0.5 mEq/L versus placebo	Placebo group declined; lithium group remained stable; memory, attention, and CSF Aβ1–42 favored lithium (Forlenza et al., 2019)	Most informative early disease-modification study; small sample and uncertain dementia-conversion inference
Gerhard et al. (2015)	Population-based claims cohort; adults ≥50 with bipolar disorder	Duration of lithium exposure versus non-use; anticonvulsants as negative control	Continuous exposure associated with lower dementia risk, HR 0.77 (Gerhard et al., 2015)	Supports preventive association; residual confounding and restricted psychiatric population
Chen et al. (2022)	Retrospective cohort; 29,618 mental-health patients ≥50	548 lithium-exposed versus unexposed	Lower risk of dementia, AD, and vascular dementia after adjustment (Chen et al., 2022)	Large real-world cohort; small exposed group and confounding by indication
Duthie et al. (2023)	Population-based Scottish cohort; 37,597 participants	Extremely low lithium in drinking water	No protective association overall; higher risk in several female low-to-intermediate exposure categories (Duthie et al., 2023)	Important negative and contradictory environmental evidence; exposure levels were extremely low and geographically measured
Gildengers et al. (2026)	Pilot randomized, double-blind feasibility trial; 80 older adults with MCI starting treatment	Two years of low-dose lithium versus placebo	No coprimary outcome reached significance; verbal recall declined more slowly with lithium; adverse events were common (Gildengers et al., 2026)	Most recent controlled test; feasibility and effect-size estimation rather than definitive efficacy

The comparison illustrates a consistent design gradient. Animal studies offer the strongest access to tissue mechanisms and pathology but have limited clinical generalizability. Observational studies provide larger samples and longer exposure but cannot fully eliminate confounding. Small randomized trials offer the best causal evidence available so far, yet their sample sizes and attrition limit precision. The 2026 feasibility trial is methodologically important because it preregistered multiple clinical, imaging, and biomarker outcomes and did not convert a suggestive single memory result into a positive overall trial.

Research Gaps

1. Dose–exposure–response relationships

The field has not established the lithium concentration that produces GSK-3β modulation or neuroprotection in the human brain. Serum targets are not equivalent to brain concentrations, and environmental exposure cannot be compared directly with oral low-dose treatment. Future trials should measure serial serum lithium, renal function, adherence, pharmacokinetics, and, where feasible, pharmacodynamic target engagement. The dose should be selected from a prespecified exposure–response model rather than borrowed from bipolar-disorder treatment.

2. Biomarker-defined disease stage

The positive MCI studies were not necessarily equivalent in amyloid status, tau burden, disease stage, or genetic risk. A prevention trial should distinguish amyloid-positive MCI, amyloid-negative MCI, subjective cognitive decline, and established AD dementia. Amyloid and tau PET, plasma p-tau, neurofilament light, CSF Aβ1–42, and structural MRI could clarify whether lithium acts on pathology, resilience, or both. The LATTICE study design included amyloid imaging, tau imaging, MRI, cognition, and plasma biomarkers, an approach that should be retained in larger trials (Gildengers et al., 2025).

3. Adequate duration and clinically meaningful endpoints

A disease-modifying effect may require years, while short trials are more likely to detect symptomatic or practice effects. Conversely, very long follow-up increases attrition and treatment crossover. Trials should define a primary clinical endpoint such as time to progression from biomarker-confirmed MCI to dementia, supported by cognitive composites and functional outcomes. Biomarker changes should be prespecified as mechanistic or secondary outcomes, not treated as substitutes for clinical benefit.

4. Replication and independent groups

The early positive randomized evidence comes largely from one research program, while the newer feasibility trial did not meet its coprimary threshold. Independent multicenter replication is necessary. Trials should use centralized randomization, blinded outcome assessment, standardized lithium monitoring, transparent handling of missing data, and independent safety oversight. Enrichment for amyloid-positive participants may improve biological specificity but could reduce generalizability.

5. Mechanism beyond GSK-3β

GSK-3β is a useful organizing hypothesis, but lithium's effects may also involve Akt, Wnt signaling, autophagy, BDNF, microRNA regulation, mitochondria, and neuron–glia interactions (A et al., 2024; Freland & Beaulieu, 2012). Future work should test mediation: does lithium-induced target engagement precede changes in tau, amyloid, inflammation, neurogenesis, or synaptic function, and do those changes predict slower cognitive decline? Without this chain of evidence, a clinical signal cannot be assigned confidently to GSK-3β inhibition.

6. Safety in the population most likely to receive treatment

Many trials select physically healthy older adults and exclude renal, cardiovascular, psychiatric, or neurological comorbidity. Real-world AD populations are more medically complex and often use diuretics, renin–angiotensin-system blockers, nonsteroidal anti-inflammatory drugs, anticoagulants, and multiple psychoactive agents. Pragmatic studies should evaluate whether low-dose strategies remain safe under realistic polypharmacy and frailty conditions. The safety endpoint should include treatment discontinuation and sustained renal or endocrine change, not only serious adverse events.

7. Comparative and combination strategies

Lithium is unlikely to replace all other AD interventions. Its multi-pathway activity could make it more useful as an early preventive agent or combination component than as monotherapy for advanced dementia. Combination trials should be undertaken only after establishing an effective and safe lithium exposure, with interaction testing against symptomatic treatments and disease-modifying antibodies. The underlying rationale is consistent with the multifactorial biology of AD, but combination therapy should not be used to obscure an unproven lithium effect.

Synthesis/Conclusion

Lithium has a credible neuroprotective rationale in Alzheimer's disease because it can influence several processes connected to neuronal vulnerability: GSK-3β and tau regulation, amyloid processing, autophagy, inflammation, oxidative and mitochondrial stress, neurotrophic signaling, and synaptic plasticity. Animal studies are broadly supportive, and early randomized MCI studies reported favorable cognitive or biomarker findings. Observational cohorts also suggest lower dementia risk among some lithium-exposed populations.

The evidence is not yet sufficient for routine lithium use to prevent or treat Alzheimer's disease. Environmental studies conflict, early clinical findings are small and concentrated in MCI, and the newest randomized feasibility trial did not meet its prespecified coprimary outcomes. The most defensible therapeutic perspective is a biomarker-guided, low-dose, closely monitored strategy tested in adequately powered multicenter trials. Until those trials demonstrate durable cognitive and functional benefit with acceptable renal, endocrine, neurological, and systemic safety, lithium should remain an investigational neuroprotective candidate rather than an established Alzheimer's treatment.

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