

THE 30-DAY BRAIN HEALTH PROTOCOL

An Evidence-Graded, Honest Guide to Lowering Dementia Risk Factors

Educational material, not medical advice. This program does not diagnose, treat, prevent, or cure Alzheimer's disease or any form of dementia. Speak with a licensed clinician before making any changes to diet, exercise, supplements, hormones, or medication, and get a professional evaluation for any new memory or thinking changes.

Who this is for: Adults who want a practical, honest, evidence-based approach to brain health — especially those with a family history of dementia, high blood pressure, high blood sugar, extra weight, poor sleep, or low fitness. Use this alongside your existing medical care, never instead of it.

Read This First

This program is a 30-day, evidence-based framework for lowering the risk factors linked to dementia.

This program is best used with our Keto 12/3 Meal Plan with recipes and our Exercise Regimen.

What This Program Is

- A structured 30-day plan built around six habit categories: food, movement, sleep, stress, social and mental engagement, and tracking a few basic health numbers
- Our best defence against Alzheimer's and dementia

What This Program Is Not

- Not individualized medical advice — This is not a replacement for a doctors visit, it does not know your labs, medications, or medical history
- Not a diagnosis — nothing here can tell you whether you have Alzheimer's disease, mild cognitive impairment, or normal aging
- Not a guaranteed prevention method — no diet, supplement, exercise plan, or program has been proven to prevent or cure Alzheimer's disease
- Not a treatment — no clinically validated lifestyle change has been shown to reverse Alzheimer's disease
- Not a replacement for your clinician — many causes of memory trouble are treatable

How to Read the Evidence Grades

Grade	What it means	Weight to give it
RCT	A randomized controlled trial — people were assigned by chance to a treatment or comparison group	Highest for cause and effect
Meta-analysis	A systematic review pooling many human studies into one estimate	Very high when pooled studies are trials
Observational	A study that watches groups over time or compares them at one moment; nobody was randomly assigned anything	Good for spotting links, weak for proving cause
Pilot	A small pilot study or case series describing a handful of patients	Hypothesis-generating only
Animal	A study in mice, rats, or other animals	Suggests mechanism, not human benefit
Lab / Mechanistic	Laboratory research, often on cells or biomarkers	Explains why something might work, not that it does
Opinion	Expert opinion, a protocol description, or a claim without adequate clinical evidence	Treat as a hypothesis

We also add strength tags where useful: (strong), (moderate), (weak), (mixed), or (negative — trial found no benefit).

The Honest Promise

Thirty days is enough time to build habits and move real, measurable numbers. Blood pressure, weight, sleep duration, aerobic fitness, and blood sugar can all shift within a month, and each of those factors is independently linked to dementia risk, according to the 2024 Lancet Commission.

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Section 1: The Bredesen Protocol, Fairly Analyzed

Dale Bredesen is a neurologist and researcher who popularized a multi-domain, personalized approach to cognitive decline, often called the ReCODE protocol. His work helped popularize the idea that brain health has multiple contributors — but this guide does not depend on his branded approach. It separates well-established actions from promising but still-developing evidence.

KetoFLEX 12/3: The Food Framework

Element	What Bredeesen says	What mainstream evidence says
"Keto"	Body shifts toward burning fat for fuel	Across 10 small trials, ketogenic approaches improved cognitive scores modestly but raised triglycerides and LDL; most used MCT supplements, not full dietary ketosis
"FLEX"	Metabolic flexibility — switching smoothly between sugar and fat as fuel	Improved flexibility helps keep insulin and glucose levels steady, lowering insulin-resistance risk
"12"	A minimum 12-hour overnight fast	When the body runs out of carbohydrate to burn, it begins burning fat
"3"	Last meal at least 3 hours before bed	A resting gut allows proper release of melatonin and human growth hormone
Longer fasts	ApoE4 carriers advised toward 16 hours by some protocol authors	Lowers insulin, encourages fat burning, often leads to natural calorie reduction
Ketosis target	BHB 1.0-4.0 mM in the original 2023 paper; a 2026 review softens this and calls ketosis "mild"	The ketogenic diet has been successful in treating obesity, type 2 diabetes, and epilepsy
Food pattern	Plant-rich, high-fiber, low glycemic load, leafy greens, berries, olive oil, nuts, low-mercury fish	Close to the Mediterranean and MIND patterns that WHO conditionally recommends
Protein	0.8-1.0 g/kg lean mass/day under age 65	Older adults with low skeletal muscle mass are roughly 60% more likely to develop dementia

Insulin sensitivity is the goal underneath all of this. Bredeesen targets fasting glucose of 70-90 mg/dL and HOMA-IR of 1.2 or less. The mainstream case for caring about blood sugar arrives from a different direction: diabetes carries a relative risk of about 1.7 for dementia.

Every Other Component, Side by Side

Component	Bredeesen's suggestion	What studies say
Exercise	At least 45 min/day; aerobic 6 days/week; strength 2/week; intervals 2/week	Regular physical exercise can reduce dementia risk by up to 41-45% and helps protect overall brain health

Sleep	7-8 hours nightly; sleep hygiene; find and treat sleep apnea	Poor sleep is linked to higher risk of cognitive decline and dementia, largely because deep sleep allows the brain to clear toxic waste proteins like beta-amyloid
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Component	Bredesen's suggestion	What studies say
Stress	HeartMath-style biofeedback 10+ min/day, plus breathing and meditation	Chronic stress helps harmful proteins build up in the brain, linked to conditions like Alzheimer's disease
Cognitive training	Brain games and training 15+ min/day, 3-6 levels/week	ACTIVE randomized 2,802 older adults with 10-year follow-up; US POINTER used BrainHQ in its winning arm; gains are mostly in the trained skills
Nutrient deficiencies	Homocysteine below 7, B12 above 500, methyl-B12/methylfolate forms	Concurrent nutrient deficiencies are associated with dementia incidence
Hormone evaluation	Full panel including cortisol, estradiol, thyroid, testosterone; bio-identical hormone therapy "when clinically indicated"	Women who used estrogen-only hormone therapy had 39% lower odds of a clinical dementia diagnosis
Inflammation	Panel of hs-CRP, IL-6, TNF-alpha; hs-CRP target under 0.9 mg/L	Systemic and brain-specific inflammation accelerates production of toxic proteins like beta-amyloid and tau
Infection	Find and treat pathogens, including valacyclovir for herpes simplex, plus tick-borne illness	Contradicted: in VALAD, herpes-positive early-AD patients on valacyclovir did worse on cognitive scores; authors do not recommend it
Toxins/environment	Test for heavy metals, organic chemicals, mold; remediate water-damaged homes	Air pollution is a recognized risk factor, and WHO's 2026 update recommends reducing household air pollution
Oral health	Oral microbiome assessed and treated	20 observational studies link gum disease to cognitive impairment (OR 1.77),
Gut health	GI evaluation and treatment; prebiotic fiber, resistant starch, fermented foods	The gut microbiome is closely linked to brain health and dementia development, particularly Alzheimer's disease

Published Criticism, Stated Fairly

Cost. Reported figures for the full ReCODE program include a \$1,399 referral fee, \$75/month subscriptions, supplements running \$150 to \$1,000/month, consults above \$300, packages up to \$10,500, and family totals above \$15,000 — one family reportedly spent \$25,000 in eight months, then stopped. Insurance generally covers little.

The counterpoint. Supporters make several points. First, the underlying idea — that dementia risk is multifactorial and attacking several factors at once beats attacking one — is now mainstream and is exactly what FINGER and US POINTER tested. Second, a randomized trial of a Bredesen-style protocol now exists, was foundation-funded, and reported large gains with only one serious adverse event judged unrelated. Third, even the leading critic agrees that aerobic exercise, a Mediterranean diet, cognitive and social engagement, and vascular risk management may benefit cognition.

Why This Guide Builds on KetoFLEX 12/3

This guide keeps KetoFLEX 12/3 as its food framework because its everyday core — plant-rich, high-fiber, low-sugar eating, an overnight fast, and no late-night meals — closely resembles the Mediterranean and MIND patterns that mainstream guidelines conditionally recommend. It is free, and it moves blood sugar, weight, and blood pressure within weeks. This guide grades every claim honestly and does not adopt strict ketone targets, grain and dairy elimination, supplement stacks, hormone therapy, or costly specialty panels, and it never calls any of it prevention.

Section 2: Food and Fasting Foundations

Bottom line: KetoFLEX 12/3 is a plant-forward, lower-carbohydrate way of eating with a 12-hour overnight fast. Its food choices overlap with the best-supported brain-healthy diets.

Four Words You Need

- **Ketosis** — when your body breaks down stored and dietary fat for fuel instead of relying mainly on sugar
- **Ketones** — the fuel molecules your liver makes from fat; the one measured in studies is beta-hydroxybutyrate (BHB)
- **Insulin resistance** — when your body stops responding well to insulin, so it must make more to do the same job
- **Metabolic flexibility** — the capacity to smoothly switch between burning glucose and burning fat for fuel

How It Is Meant to Work

The published description is plant-rich but not plant-exclusive, high in fiber, mildly ketogenic, low in glycemic load, heavy on leafy greens and non-starchy vegetables, and high in unsaturated fats. Vegetables form the base of the plate, healthy fats supply most calories, and protein is adequate but not extreme.

The claimed effects are broad: insulin sensitivity, better fuel supply to neurons, improved mitochondrial function, less inflammation, and raw materials for synapses. The "brain fuel" idea has a mechanistic anchor — PET scans show the brain takes up ketones when they're available — but that is uptake, not proof that a fuel shortfall was corrected. No randomized trial of KetoFLEX 12/3 as a whole exists.

Is Deep Ketosis Necessary? No.

Deep ketosis is not needed. A ketogenic pilot in Alzheimer's research counted people as adherent above a BHB of just 0.3 mmol/L. A 6-month randomized trial raised brain ketone metabolism by 230% using 30 g/day of MCT oil (medium-chain triglyceride, a fat the liver converts to ketones quickly) with no carbohydrate restriction at all. Treat mild ketosis as an optional, evidence-thin accelerator, never a requirement — the route with the most randomized support is modest MCT oil, discussed with your clinician, not deep sustained ketosis.

The 12-Hour Fast: What Holds Up

- Animal and pilot studies from institutions including the National Institute on Aging show promising cognitive improvements and reduced brain damage in mice using time-restricted feeding
- Preliminary human data suggests time-restricted eating may improve spatial planning and memory, though it has not yet been tested for its effect on sleep in people with Alzheimer's disease
- Longer fasts may not be safe for everyone — especially older adults, people with a low BMI, or those managing diabetes with insulin

Why "3 hours before bed" matters: in a randomized crossover study, 20 healthy young adults ate an identical dinner at 6 p.m. or 10 p.m. The late dinner produced higher blood glucose, a delayed triglyceride peak, less burning of dietary fat, and higher cortisol.

Autophagy. Autophagy is the cell's recycling process, clearing out damaged parts. In Alzheimer's disease, disruption of autophagy contributes to hallmark pathology including amyloid accumulation, tau hyperphosphorylation, and progressive neurodegeneration. Most evidence suggests autophagy begins somewhere between 24 and 48 hours of fasting, though this estimate comes primarily from animal studies — there is no confirmed hour mark in humans.

Benefits and risks. The 12-hour fast is simple, free, and crowds out late-night snacking; mild fasting was described as safe in cognition reviews. But the muscle signal is real: twelve weeks of a stricter 16:8 schedule caused significantly greater loss of appendicular lean mass (the muscle in your arms and legs) than structured meal timing. Never attempt extended or multi-day fasting on your own — ask your clinician about any fast longer than the 12-hour overnight window.

A Safe 4-Week Transition Ramp

This ramp is for someone eating a standard diet now. No macronutrient, calorie, or carbohydrate targets are published for KetoFLEX 12/3, so the steps below are a conservative ramp, not trial numbers. If you take insulin, a sulfonyleurea, an SGLT2 inhibitor, or blood-pressure medication, talk to your clinician first.

Week	Focus	What to do
1	Timing only	Finish dinner 3+ hours before bed; leave 12 hours before breakfast. Change nothing else about what you eat. Drink water with meals; salt food as usual unless told to restrict sodium. Weigh yourself once and write it down.
2	Crowd in vegetables, fiber, protein	Make non-starchy vegetables the biggest thing on the plate at two meals daily (asparagus, broccoli, brussels sprouts, cabbage, cucumbers, zucchini). Add leafy greens daily and berries most days. Hit your protein target every meal: protein first, then vegetables, then fat. Raise fiber from vegetables, nuts, seeds, and legumes.

3	Remove the biggest offenders	Cut added sugar, sugar-sweetened drinks, refined grains, and packaged snacks. Replace with unprocessed food — this swap has the best data of anything in this guide. Use olive oil, avocado, olives, nuts, and seeds as replacement calories. Watch electrolytes; as carbohydrate falls, headache and fatigue are common.
4	Settle, don't tighten	Hold the pattern. Do not extend the fast past 12 hours or chase ketone readings. Resistance train twice a week — not optional for an older adult cutting carbohydrate. Re-weigh; if you lost weight, eat more food, not less. Book blood work, including lipids.

Protein, Fiber, and Hydration

Protein. Older adults with low skeletal muscle mass are roughly 60% more likely to develop dementia. Bredesen's suggestion is 0.8-1.0 g/kg of lean mass daily under age 65, higher above 65 to counter age-related muscle loss. The 2025-2030 Dietary Guidelines for Americans suggest a broader adult range of 1.2-1.6 g/kg body weight daily — in plain terms, roughly 0.4-0.7 grams per pound. Where you land depends on age, activity, and weight goals.

Fiber. The pattern is explicitly high-fiber. No single confirmed gram target for older adults specifically was found in the sources reviewed; the practical rule is that fiber should rise as refined carbohydrate falls, from vegetables, legumes, nuts, and seeds.

Hydration and electrolytes. Drink to thirst and keep fluids visible during the day. Coffee, tea, or matcha are fine earlier in the day, but caffeine after lunch can disrupt sleep — water or sparkling water are better evening choices. Consider stopping fluids an hour before bed to protect uninterrupted sleep, since sleep quality itself is one of the more important levers in this guide.

"Keto flu." Some people feel unwell in the first weeks of lower-carbohydrate eating — headache, fatigue, GI upset. Pooled data across ketogenic trials show at least one adverse event in roughly 43% of participants, most commonly gastrointestinal. To avoid it: ramp over four weeks, don't chase deep ketosis, keep fluids and salt adequate, keep fiber high, and eat enough food overall.

Food Quality: What Goes on the Plate

Bottom line: if you do one thing, replace ultra-processed food with real food.

Food group	Evidence
Leafy greens and non-starchy vegetables	Roughly half a cup of cooked greens or one cup of raw salad daily was linked to slower cognitive decline in a large observational cohort (Rush Memory and Aging Project)
Cruciferous and allium vegetables	Broccoli, cabbage, garlic, and onions carry some of the strongest single-food links in dietary-pattern research
Berries	Berries and leafy greens are the two food groups that distinguish MIND-diet scoring from Mediterranean and DASH scoring

Olive oil	The only ingredient in this framework with randomized trial support; linked to a modest cognitive score improvement in PREDIMED-style trials
Nuts and seeds	Part of both Mediterranean and MIND scoring; support healthy fat intake and satiety
Low-mercury fish	Omega-3-rich fish is part of the base pattern; mercury exposure itself is a separate, unrelated caution for very high-mercury species
Ultra-processed food	Swapping just 10% of ultra-processed food for minimally processed alternatives was linked to notably lower dementia risk in a large biobank study
Fermented foods	Emerging interest via the gut-brain axis; no dementia-specific trial confirmed

Section 3: The Lifestyle Evidence Map

Bottom line: the biggest expert bodies now agree that a large share of dementia risk is linked to things you can act on.

The Lancet Commission: 14 Modifiable Risk Factors

The 2024 Lancet Commission on Dementia Prevention, Intervention and Care identified 14 potentially modifiable risk factors accounting for a weighted population attributable fraction (PAF) of 45.3% of dementia cases worldwide. PAF is a population-level estimate: if a risk factor were completely removed from the whole population, what share of cases might not happen? It assumes the link is causal, which is not fully settled for every factor.

Life stage	Risk factor	Relative risk	Weighted PAF
Early life	Less education	1.6	5%
Midlife	Hearing loss	1.4	7%
Midlife	High LDL cholesterol	1.3	7%
Midlife	Depression	2.2	3%
Midlife	Traumatic brain injury	1.7	3%
Midlife	Physical inactivity	1.2	2%
Midlife	Smoking	1.3	2%

Midlife	Diabetes	1.7	2%
Midlife	Hypertension	1.2	2%
Midlife	Obesity	1.3	1%
Midlife	Excessive alcohol	1.2	1%
Late life	Social isolation	1.6	5%
Late life	Air pollution	1.1	3%
Late life	Untreated vision loss	1.5	2%

Two honest notes: the relative risks are mostly small — 1.2 means about a 20% higher rate, not a doubling — and every row rests on observational data, which can be shifted by confounding and reverse causation.

What the Major Health Authorities Recommend

Domain	WHO recommendation	Strength
Physical activity	Recommended for adults with normal cognition to reduce decline risk	Strong
Tobacco	Offer cessation help to all tobacco users	Strong
Diet	Mediterranean-like or healthy balanced diet	Conditional to strong
Supplements	Vitamins B/E, omega-3s, multivitamins should not be used for risk reduction	Strong (against)
Hypertension / diabetes	Manage per existing WHO clinical guidelines	Strong

Domain	WHO recommendation	Strength
Cognitive training / social activity	Now recommended as of the 2026 update	Conditional
Hormone therapy	Recommended against, specifically for dementia risk reduction	Strong (against)

Household air pollution	Reduce exposure where feasible	Conditional (new in 2026)
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The Alzheimer's Association's consumer list, 10 Healthy Habits for Your Brain, echoes this: challenge your mind, stay in school, get moving, protect your head, be smoke-free, control your blood pressure, manage diabetes, eat right, maintain a healthy weight, and sleep well.

Blood Pressure and Vascular Health

This is the single best-supported medical lever in this entire guide. The brain runs on a dense network of small blood vessels — damage them and you get vascular injury linked to higher rates of Alzheimer's-type diagnoses. The 2025 AHA/ACC guideline makes a Class 1 recommendation: in adults with hypertension, a systolic blood pressure goal of 130 mm Hg is recommended specifically to help prevent mild cognitive impairment and dementia.

The landmark SPRINT MIND trial randomized 9,361 adults 50 and over to a systolic target below 120 versus below 140 mm Hg. Probable dementia occurred in 248 vs 293 cases (HR 0.86, $p=0.08$) — short of statistical significance. But mild cognitive impairment was significantly reduced (380 vs 430 cases, HR 0.87, $p=0.04$), as was the combined MCI-or-dementia endpoint (555 vs 622 cases, HR 0.89, $p=0.04$). Pooled across 14 trials and over 96,000 participants, blood-pressure lowering reduced dementia or cognitive impairment with an odds ratio of 0.93 — consistent but modest, an absolute reduction of well under 1%.

Your job during these 30 days is measurement, not medication changes — bring your blood pressure log to your clinician.

Exercise and Physical Resilience

Physical activity carries WHO's strongest possible rating: recommended to adults with normal cognition to reduce decline risk. In one large observational study of nearly 80,000 adults, roughly 9,800 steps a day was linked to significantly lower dementia risk — and even 3,800 steps a day showed meaningful benefit. Regular physical exercise has been linked to reductions in dementia risk as high as 41-45% in some meta-analyses.

The honest half: trials using cognition as the primary outcome have mostly come back null. But strength training still earns its place — low grip strength is linked to dementia risk, structured exercise cuts fall risk by roughly 23%, and head injury is itself an independent risk factor, making fall prevention doubly important.

Sleep

The American Heart Association sets the adult sleep target at 7 to 9 hours nightly as one of its eight core health metrics. Deep sleep specifically allows the glymphatic system to clear waste proteins, including beta-amyloid, from brain tissue — a mechanistic reason sleep quality (not just duration) matters.

Be clear on the grade: WHO judged sleep evidence insufficient for a strong 2026 recommendation, and the National Institute on Aging places sleep in its "some but not as much evidence" tier. Sleep still earns its place in this protocol because it's free, safe, supports every other habit, and poor sleep is the doorway to sleep apnea — a condition linked to heart disease, diabetes, and cognitive impairment.

Senses: Hearing and Vision

Hearing loss carries a relative risk of 1.4 and a 7% weighted PAF in the Lancet Commission analysis — the single largest modifiable midlife factor identified. Untreated vision loss adds another 2% weighted PAF at late life. Both are straightforward to screen for and treat, making them some of the highest-leverage, lowest-effort actions in this guide — though note that the large ACHIEVE hearing-aid trial found no overall cognitive benefit, only in a higher-risk subgroup.

Mind, Mood, and Connection

Depression carries the highest single relative risk in the Lancet analysis (2.2), and social isolation carries a relative risk of 1.6 with a 5% weighted PAF. The 2026 WHO update newly recommends cognitive training, cognitive stimulation, and social engagement — a shift from 2019, when social-factor evidence was judged

insufficient. Combined, these form the "multidomain" pattern tested by FINGER and US POINTER — real benefit, but modest in size. In ACTIVE, a 10-year randomized trial of 2,802 older adults, cognitive training produced durable gains mostly confined to the specific trained skill.

Section 4: Environmental and Medical Risk Factors

Bottom line: several every day, non-dietary factors carry real evidence, ranked here from most to least actionable.

Oral and Periodontal Health

Periodontitis is gum disease advanced enough to damage the tissue and bone holding teeth. Chronic gum infection produces body-wide inflammation, and the bacterium *Porphyromonas gingivalis* releases enzymes called gingipains that some researchers propose can reach the brain.

Finding	Design	Effect
Periodontitis and cognitive impairment	Meta-analysis, 20 observational studies	OR 1.77 (1.31-2.38)
Periodontitis and dementia, all severities	Same meta-analysis, 11 studies	OR 1.59 (0.92-2.76) — not significant
Moderate/severe periodontitis and dementia	Subgroup	OR 2.13 (1.25-3.64)
Periodontal disease and dementia	Systematic review, 46 records	RR 1.22 (1.10-1.36)
Periodontal disease and dementia	7 cohorts, 226,628 patients, 8 yrs	RR 1.38 (1.01-1.90)
Oral-hygiene behaviors	8 studies, 261,772 participants	Toothbrushing linked to slower decline; flossing/mouthwash not linked

An umbrella review of 8 reviews found poor oral health — plaque, gingival bleeding, periodontal disease — consistently associated with worse cognitive outcomes, though no trial shows that treating gum disease changes cognition. The practical takeaway: normal dental hygiene and regular cleanings are a reasonable, low-cost, low-risk addition to this protocol.

Air Pollution

Air pollution is a Lancet risk factor with relative risk 1.1 and a 3% weighted PAF. A systematic review of 28 longitudinal cohorts found a minimum 14% increased dementia risk across fine-particle (PM_{2.5}) levels of 4.5 to 26.9 µg/m³ versus a 2.0 reference — though the authors rated their own confidence at two stars out of five for dementia, and vascular dementia showed no significant association. Modeling attributes roughly 3% of global dementia cases, about 1.65 million, to air pollution.

Two nuances worth knowing. Living within 50 meters of a major road versus more than 300 meters carried a hazard ratio of 1.07 in about 2.2 million Ontario adults — real, but very small. And wildfire-specific PM_{2.5} was not significantly associated with dementia in 1.2 million Kaiser Permanente members, while ordinary non-wildfire PM_{2.5} was.

A brain-tissue study of 602 donated brains found that for every 1 µg/m³ increase in lifetime-average PM_{2.5}, researchers observed 19% higher odds of more severe overall Alzheimer's pathology, 17% higher odds of more amyloid buildup, and 20% higher odds of worse tau pathology and amyloid plaque burden, plus 16% higher odds of a large brain infarct. Importantly, "19% higher odds" describes a shift in the odds of a more severe pathology category among the people studied — not a 19% higher chance of getting Alzheimer's. Among roughly 287 people with detailed cognitive testing, higher pollution exposure was also linked to worse memory and daily function, and about 63% of that link was statistically explained by increased Alzheimer's brain pathology.

Practical action: a bedroom HEPA filter and good kitchen ventilation are low-cost, low-risk, and have proven benefits for respiratory health even though the dementia-specific effect size is small.

Pesticides, Solvents, and Heavy Metals

Exposure	Evidence	Effect
Pesticides and Alzheimer's	Meta-analysis, 7 studies, 6,835 people, 1,050 cases	OR 1.34 (1.08-1.67); higher-quality studies OR 1.42
Nearby agricultural organophosphates	Prospective cohort, n=430, 6.5 years	Faster cognitive decline (p=0.021); dementia HR 1.94 (0.75-5.03, not significant)
Solvents and small-vessel/vascular dementia	Systematic review, 85 populations, 47,743 people	Pooled effect on vascular dementia could not be confirmed
Aluminum	Historical review of animal, brain-tissue, and dialysis data	The role of aluminum in Alzheimer's disease remains contentious

On lead, official guidance is clear and actionable: there is no known safe blood-lead level in children, the drinking-water action level is 15 parts per billion, a home water test costs \$20-\$100, and boiling does not remove lead — use only cold water for drinking and cooking, filtered if your home has pre-1986 plumbing or a private well. For mercury, the FDA and EPA advise 2-3 servings a week from the "Best Choices" fish list; for self-caught fish with no local advisory, limit to one serving weekly.

Practical actions: follow the fish guidance, wash produce, cut household pesticide use, ventilate and wear protection when using solvents rather than planning to "detox" later, and test tap water if you have pre-1986 plumbing or a private well.

Chronic Infections and Vaccines

Much of this evidence comes from natural experiments — real-world situations where something close to random assignment happened by accident, such as a vaccine eligibility cutoff based on birth date.

Finding	Design	Effect
Shingles (zoster) vaccine, Welsh natural experiment	Regression discontinuity, Sept 2 1933 birth-date cutoff, 282,541 adults	New dementia diagnosis reduced 8.5% relative ($p=0.022$) for eligibility; 20.0% relative ($p=0.019$) for actually receiving it
Recombinant (Shingrix) vs. live shingles vaccine	Natural experiment on the rapid US switch, 6-year follow-up	Recombinant linked to 17% increase in diagnosis-free time — about 164 extra days without a dementia diagnosis; larger effect in women
Vaccination overall (zoster, flu, pneumococcal, Tdap)	Meta-analysis, 21 studies, 104,031,186 participants	Zoster: RR 0.76 for any dementia, RR 0.53 for Alzheimer's; flu: RR 0.87; pneumococcal: RR 0.64 for Alzheimer's; Tdap: RR 0.67
Symptomatic herpes simplex infection	87,687 patients vs 217,895 matched controls	HR 0.80 — lower dementia risk, the opposite of an infection-causes-dementia story
COVID-19 and cognition	Prospective cohort, $n=3,525$, global	Hospitalized infection: small excess cognitive change; non-hospitalized: no excess decline
Lyme neuroborreliosis	Danish cohort, 2,067 patients vs 20,670 comparators	Dementia HR 0.89 (0.60-1.31) — no increased risk
Chlamydia pneumoniae	Narrative review	"Remains controversial"

A 2025 meta-analysis concluded: adult vaccination — particularly against herpes zoster, influenza, pneumococcus, and Tdap — is associated with lower dementia risk, and vaccination strategies should be

considered part of public health dementia-prevention initiatives. This is association, not a randomized proof of causation, but the consistency across natural experiments and large meta-analyses makes it one of the stronger observational signals in this guide. Staying current on adult vaccines is a low-risk, low-cost, broadly beneficial action regardless of the dementia link.

Gut Microbiome

Research suggests the gut microbiome may play a role in Alzheimer's development or progression. An unhealthy or imbalanced gut microbiome may increase intestinal permeability, inflammation, and exposure to bacterial toxins, which could contribute to brain inflammation, disruption of the blood-brain barrier, and changes related to amyloid buildup. People with Alzheimer's often show different gut bacterial patterns than cognitively healthy people, though researchers have not determined whether these changes help cause Alzheimer's or occur as a result of it.

Researchers are studying whether improving gut health through diet, prebiotics, probiotics, and other microbiome-targeted treatments could reduce cognitive decline. The evidence is promising but preliminary, and no specific probiotic or microbiome treatment has been proven to prevent Alzheimer's. For now, a high-fiber, plant-rich diet, fermented foods, regular exercise, and avoiding unnecessary antibiotics is a reasonable strategy with broad health benefits beyond any dementia-specific claim.

Section 5: Emerging and Controversial Approaches

Bottom line: these are legitimate areas of active research, not proven prevention tools. None are required for this protocol.

40Hz Light and Sound Stimulation

Gamma-frequency (40Hz) sensory stimulation is an emerging research area. Animal studies suggest reduced Alzheimer-related pathology, and small human studies in mild cognitive impairment or early Alzheimer's suggest daily 40Hz light-and-sound stimulation is feasible, generally well tolerated, and may slow cognitive and functional decline. It is not yet a proven prevention or treatment and should not replace medical care. People with seizure disorders, light sensitivity, or certain neurologic conditions should get clinician guidance before trying flashing-light devices.

Frequent Sauna Bathing

Finnish observational studies found more frequent sauna use associated with lower later dementia and Alzheimer's risk. This is an association, not proof that sauna causes protection — sauna users may differ from non-users in other important ways (income, baseline fitness, social patterns). If you enjoy a sauna and your clinician says it's safe, use hydration, avoid alcohol, stop if dizzy or unwell, and avoid it when acutely ill or medically contraindicated.

Hyperbaric Oxygen Therapy

A 2024 systematic review and meta-analysis included 11 randomized controlled trials with 847 people with Alzheimer's disease and found improvements on cognitive and daily-function scales among participants receiving hyperbaric oxygen. The authors called the findings promising while calling for more rigorous studies to define its true clinical value — this is not yet a validated standard of care.

What's Established vs. Speculative — Reread This Before Spending Money

Claim or product	Status	What the evidence actually says
Fixing dampness and leaks in your home	Established as a general health measure	Dampness affects 10-50% of indoor environments and raises respiratory symptoms, infections, and asthma flare-ups; no dementia outcome has been studied directly
Testing tap water for lead with pre-1986 plumbing or a well	Established and actionable	Action level 15 ppb; test costs \$20-\$100; boiling does not remove lead

How to Rank All of This in Your Own Life

Priority	Actions	Why
First	Blood pressure, physical activity, tobacco, diabetes and cholesterol care	The only areas with strong WHO ratings and randomized-trial support
Second	Hearing and vision checks, sleep-apnea evaluation if symptomatic, depression screening, dental care, adult vaccines	Large PAFs or Grade B screening, with clear benefits beyond brain health
Third	Bedroom HEPA filter, kitchen venting, damp repair, water testing, fiber and fermented foods	Low risk, proven intermediate effects, but unproven dementia-specific effect

Section 6: Hormones and Prescription Medicines

This is education, not medical advice. Anyone noticing memory or thinking changes should get a professional medical evaluation. Never start or stop a prescription based on this program.

Part 1: Hormones, a Careful and Balanced Review Discuss with your doctor

Estrogen, progesterone, testosterone, and thyroid hormone all act on brain cells — that biology is real.

Estrogen therapy. A 2023 review looked at whether estrogen therapy protects women against Alzheimer's and dementia after menopause and concluded estrogen appears to have several potentially protective effects, including reducing inflammation and oxidative stress and supporting memory-related brain regions. Timing matters: estrogen therapy may be more beneficial when started around perimenopause or within the first several years after menopause rather than much later. Progesterone is usually taken alongside estrogen to lower cancer risk. Human evidence remains mixed, and the 2026 WHO guideline recommends against hormone therapy specifically for dementia risk reduction.

Thyroid hormone. Recent studies show a significant link between thyroid hormone levels and dementia risk. Adults 65 and older with a history of hypothyroidism have an increased dementia risk, with some studies

reporting an 81% higher risk. Those requiring thyroid hormone replacement therapy face an even greater risk, suggesting thyroid dysfunction may play a role in cognitive decline. This makes routine TSH testing worthwhile, even though USPSTF gives it an "I" (insufficient evidence) statement for screening and treating purely to improve cognition.

Testosterone. Higher plasma testosterone concentration was associated with worse cognition in some studies, while higher testosterone was separately linked to fewer behavioral and psychological symptoms — a genuinely mixed picture that does not support supplementation for brain health.

Part 2: Prescription Medicines — Clinician-Managed Options Only

Bottom line: no prescription drug is approved anywhere to prevent dementia in the general population.

Everything below is a question for a prescriber, never an instruction. Hold on to one distinction: association means people who take a drug happen to get less dementia, which may be caused by the drug or by the kind of person who takes it. Proven prevention means a randomized trial assigned the drug at random and dementia went down. Almost everything below is the first kind.

Blood-Pressure Medicines

Lowering blood pressure reduces damage to small brain vessels, white-matter injury, and stroke. Across five placebo-controlled trials, 53% of the benefit was attributable to the blood-pressure drop itself (range 27-76%). SPRINT MIND randomized 9,361 adults 50+ to a systolic target below 120 vs below 140.

Endpoint (median 6.9 yrs)	Result
Probable dementia	248 vs 293 cases; HR 0.86 (0.72-1.02), p=0.08
Mild cognitive impairment	380 vs 430 cases; HR 0.87 (0.76-1.00), p=0.04
MCI or probable dementia	555 vs 622 cases; HR 0.89 (0.79-0.99), p=0.04

Pooled across 14 trials and 96,158 participants, dementia or cognitive impairment showed OR 0.93 (0.88-0.98) — an absolute reduction of just 0.39%. Consistent, but modest.

Statins and Other Lipid-Lowering Drugs

This is the clearest lesson in the difference between association and proof.

Design	Result
Observational meta-analysis, 55 studies, over 7M patients	Dementia HR 0.86 (0.82-0.91)
Cochrane review of randomized trials, 26,340 participants	Incident dementia OR 1.00 (0.61-1.65) — negative

An apparent 14% reduction in observational data becomes zero when people are randomized, because statin users are healthier, more adherent, and live longer. The PROSPER trial found no effect in any cognitive domain. On the flip side, concern that statins harm memory doesn't hold up either: drug labels note rare,

reversible postmarketing reports, and a meta-analysis of 27,643 people found cognitive scores differed by only 0.01 standardized units. PCSK9 inhibitors showed no cognitive difference from placebo in the EBBINGHAUS trial.

Diabetes Medicines

- **Metformin** — of 17 observational studies, 11 reported reduced dementia risk, but all 17 had time-related bias; the two studies addressing that bias most rigorously found no significant association. A larger 2024 design found metformin was not associated with incident dementia. The randomized METFINGER trial is still enrolling with no results yet
- **Pioglitazone** — tested in a randomized trial of 3,494 cognitively healthy adults 65-83; 2.7% vs 3.3% developed MCI due to Alzheimer's (HR 0.80, not significant), and the trial stopped for futility. It also carries fluid-retention and historical bladder-cancer concerns
- **SGLT2 inhibitors** — in 110,885 matched Korean pairs, SGLT2 starters vs DPP4 starters had dementia HR 0.65 (0.58-0.73), the best observational signal in diabetes care — but follow-up averaged only 1.8 years and this compares two drugs, not drug versus no drug. No randomized cognitive trial exists
- **GLP-1 receptor agonists (including EVOKE)** — GLP-1 receptors exist in the brain, and semaglutide cut major cardiovascular events by 20% in the SELECT trial. But EVOKE and EVOKE+ randomized 3,808 adults 55-85 with biomarker-confirmed MCI or mild Alzheimer's to oral semaglutide or placebo for two years; neither trial showed statistically significant slowing of progression, and the planned extension was discontinued. A cohort study found dementia HR 0.63, but follow-up was only 1.77 years with a large mortality gap suggesting confounding

Medications to Reconsider With Age (Anticholinergic Burden)

The 2023 American Geriatrics Society (AGS) Beers Criteria flag several drug classes as potentially inappropriate for adults 65 and over. "Potentially inappropriate" is not an absolute ban — the criteria should not be simplified as "avoid in everyone over 65."

Drug group	Recommendation and rationale
First-generation antihistamines (diphenhydramine, chlorpheniramine, hydroxyzine, meclizine, promethazine, doxylamine)	Avoid. Cumulative exposure to anticholinergic drugs is associated with increased risk of falls, delirium, and dementia, even in younger adults
Strongly anticholinergic antidepressants (amitriptyline, doxepin over 6mg/day, imipramine, nortriptyline, paroxetine)	Avoid. Highly anticholinergic, sedating, and cause orthostatic blood-pressure drops
Any anticholinergic in someone with dementia, especially multiple at once	Avoid; minimize the number. Multiple anticholinergics increase cognitive decline, delirium, and falls or fractures
Benzodiazepines	Avoid generally — all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor-vehicle crashes in older adults. May still fit seizure disorders, REM sleep behavior disorder, withdrawal, or procedures

The action is not "stop your medication." It is to bring your full medication and supplement list, including over-the-counter sleep aids and allergy pills, to a scheduled review with your prescriber or

pharmacist.

Aspirin, NSAIDs, and Antivirals — All Tested, All Failed

Drug	Trial	Result
Aspirin 100mg/day	ASPREE, 19,114 adults 70+	All dementia HR 1.03 (0.91-1.17); probable Alzheimer's 0.96; major bleeding increased — negative
Naproxen and celecoxib	ADAPT, 2,528 adults 70+ with family history	Celecoxib HR 1.03; naproxen HR 0.92 — negative
Valacyclovir 4g/day	VALAD, 120 adults with early Alzheimer's	Cognition worsened more on valacyclovir (p=0.01); authors say "not recommended" — negative

Aspirin should not be taken for brain health. No completed randomized trial of antibiotics for dementia could be confirmed, and nothing supports antibiotic use for cognitive reasons.

Putting the Medication Picture Together

- Nothing here is a validated dementia-prevention pill. The only randomized evidence pointing toward reduced dementia comes from blood-pressure lowering, and even there the strongest signal is on mild cognitive impairment, not full dementia
- Treatment is not prevention. Lecanemab and donanemab modestly slow measured decline in confirmed early Alzheimer's, at meaningful ARIA (brain swelling/bleeding) risk. Cholinesterase inhibitors and memantine give small symptomatic benefit and do not change the underlying disease
- Well-publicized candidates failed randomized tests: oral semaglutide, pioglitazone, aspirin, NSAIDs, valacyclovir. Observational "protective" signals for metformin, SGLT2 inhibitors, statins, and GLP-1 drugs remain association only
- The most actionable medication lever is subtraction, not addition — a clinician-led review of anticholinergic burden, sedatives, and antipsychotic use

Never start or stop a prescription based on this program. Every item in this section is a question to bring to your prescriber, not an instruction. Stopping benzodiazepines, gabapentinoids, antipsychotics, opioids, or proton pump inhibitors abruptly can cause serious harm.

Section 7: Tracking Your Numbers

Bottom line: you don't need a lab to start. A handful of simple, at-home numbers give you real feedback within days.

Blood Pressure

This is the highest-value number in this entire guide. Measure it twice daily, sitting, after 5 minutes of rest, using a validated home cuff, averaging two readings per occasion. A single reading is inadequate for clinical decision-making — what matters is the pattern over days and weeks. Target: systolic at or below 130 mm Hg from age 40 onward, per both the Lancet Commission and the 2025 AHA/ACC guideline.

Blood Sugar

Test	What it measures	When to check	Healthy target range*
Fasting glucose	Blood sugar after 8+ hours without food, via finger-stick glucometer	First thing in the morning, before eating	70-90 mg/dL
Post-meal glucose	How high blood sugar rises after eating	1-2 hours after a meal	Under 140 mg/dL
HbA1c	Average blood sugar over roughly 3 months, via lab blood draw	Every 3-6 months, or at your annual physical	Under 5.7% (prediabetes 5.7-6.4%, diabetes 6.5%+)
HOMA-IR	A calculated estimate of insulin resistance from fasting glucose and insulin	At a lab visit, ask your clinician to calculate it	1.2 or below

*These ranges reflect general healthy-adult targets discussed in the source material, not a personalized medical target. Diabetes carries a relative risk of roughly 1.7 for dementia. A home glucometer costs \$20-\$40 and test strips are sold at any pharmacy — no prescription needed for most models. Continuous glucose monitors (CGMs) in non-diabetics are speculative for dementia purposes: a review found they "show promise for personalizing lifestyle interventions" but impact on hard outcomes "remains limited," with no dementia-specific evidence.

Ketones

Method	What it measures	Convenience	Notes
Blood ketone meter (BHB)	Beta-hydroxybutyrate level in blood, in mmol/L	Requires a finger-stick strip; most accurate	Mild ketosis in research ranged from 0.3 to 4.0 mmol/L — deep ketosis is not required for benefit
Urine ketone strips	Acetoacetate excreted in urine	Cheapest, least invasive	Less accurate over time as the body adapts to burning fat; best for early tracking only
Breath ketone meter	Acetone in exhaled breath	Reusable device, no strips needed	Moderate accuracy; convenient for daily spot checks

If you choose to track ketones at all, remember this guide's position: mild ketosis is an optional, evidence-thin accelerator — not a requirement. A pilot study in Alzheimer's research counted people as "adherent" at a BHB of just 0.3 mmol/L. There is no need to chase higher numbers.

Other Numbers Worth Tracking

- **Weight and waist circumference** — waist cutpoints of 102 cm (40 in) for men and 88 cm (35 in) for women flag higher metabolic risk; BMI 30+ adds risk
- **Sleep duration and consistency** — a wearable or simple log of bedtime/wake time; target 7-9 hours on a consistent schedule
- **Steps per day** — a pedometer or phone app; benefit observed even at 3,800 steps/day, stronger near 9,800
- **LDL cholesterol, ApoB, and Lp(a)** — require a lab blood draw; LDL 160+ is risk-enhancing, 190+ severe; ApoB 130+ and Lp(a) 50+ are selective risk-enhancers
- **hs-CRP (inflammation)** — a lab blood draw; not a guideline dementia screen, but a general marker of systemic inflammation

Section 8: The 30-Day Implementation Plan

Habits move first: in the French MAPT trial, lifestyle-arm participants raised activity by at least 300 MET-minutes per week within 6 months, and the difference held at years 2 and 3. Second, some numbers do move in a month: blood pressure, waist, sleep timing, steps, eating window. Third, you get a clean baseline and a clinician conversation you may have been putting off.

This program rests on five pillars, in order of evidence strength: managing your numbers (especially blood pressure), moving your body daily, eating the KetoFLEX 12/3 way, protecting sleep, and training your brain while staying socially connected.

Week-by-Week Plan

Week	Theme	Key actions
1	Baseline and setup	Record blood pressure twice daily. Measure waist circumference. Log your eating window, bedtime, and steps for 7 days without changing them. Move to a gentle 12-hour overnight fast. Book a clinician visit and a dental checkup.
2	Build structure	Hold the 12-hour fast; move your last bite to 3+ hours before bed. Start your aerobic target and add two strength sessions. Set a fixed wake time. Swap 10% of ultra-processed food for whole food. Add greens, berries, nuts, and olive oil most days. Confirm vaccinations are current.
3	Deepen the habit	Make cognitive activity genuinely effortful — a new language, instrument, or course. Break up long sitting periods. Push toward 6,000-10,000 steps daily. Check protein intake against your target. Add a HEPA filter to your bedroom if air quality is a concern.
4	Consolidate and plan	Re-measure blood pressure, waist, sleep, and steps; compare with Week 1. Drop any add-on you didn't enjoy — a habit you abandon is worth nothing. Choose two actions to hold for a full year. Write your Day 31 plan.

Your Daily Checklist

- Ate the KetoFLEX 12/3 way — 12-hour fast, last bite 3+ hours before bed
- Moved my body today (aerobic or strength, per the weekly target)
- Protected 7-9 hours of sleep on a consistent schedule
- Did one genuinely hard cognitive task and had one real social contact
- Logged my numbers (blood pressure, and blood sugar/ketones if tracking)
- Brushed and flossed; kept up basic oral hygiene

Do NOT Start These On Your Own

Every item below belongs in a "discuss with a clinician first" category. None are required for this 30-day program, and starting any without medical supervision can be unsafe.

Do not self-start	Why — discuss with a clinician instead
Hormone therapy (including menopausal)	The 2026 WHO guideline recommends against it specifically for dementia risk reduction; menopause symptoms should be evaluated on their own merits
Any new prescription medication	Insulin, sulfonylureas, SGLT2 inhibitors, and blood-pressure medications all need physician-guided dose adjustments alongside dietary changes
Extended or multi-day fasting	A 16:8 schedule was linked to greater muscle loss than 12-hour fasting in trials; longer fasts need clinical supervision
High-dose supplements or IV therapy	WHO recommends against B/E vitamins, omega-3s, and multivitamins for dementia risk reduction without a diagnosed deficiency
Heavy-metal chelation or "detox" protocols	Not supported by mainstream evidence for dementia risk reduction and carries real medical risk
Intense new exercise programs (if previously sedentary)	Get medical clearance first, especially with cardiovascular, joint, or blood-pressure conditions
Valacyclovir or other antivirals for cognitive reasons	The VALAD trial found cognition worsened more on valacyclovir; not recommended by trial authors
Aspirin or NSAIDs for brain health	ASPREE and ADAPT both found no benefit and increased bleeding risk with aspirin

Section 9: Baseline Medical Evaluation

Almost nothing here is a dementia test. These are general-health tests for risk factors linked to dementia — a different and more honest claim. The US Preventive Services Task Force gives an "I" statement — insufficient evidence — for screening symptom-free older adults for cognitive impairment itself. That does not mean harmful; it means nobody has shown it helps.

Table A: Routine, Evidence-Based Testing

Test	Why it matters	Reference target
Blood pressure	The only guideline aimed directly at dementia	Normal 120/80; Class 1 target 130 systolic to prevent MCI/dementia; average 2 readings, 2 occasions
Waist and body composition	Midlife obesity: relative risk 1.3	102cm men, 88cm women; BMI 30+
Fasting glucose	Diabetes: relative risk 1.7	Prediabetes 100-125 mg/dL; diabetes 126+
HbA1c	Average blood sugar over 3 months	Prediabetes 5.7-6.4%; diabetes 6.5%+; screen from age 35
Fasting insulin / HOMA-IR	Looks for insulin resistance	Not a guideline screen; no validated cutoff
Lipid panel	High LDL: relative risk 1.3	LDL 160+ risk-enhancing, 190+ severe; ApoB 130+, Lp(a) 50+ selective
Thyroid TSH	Can mimic cognitive symptoms	0.4-4.5 mIU/L; USPSTF I statement on cognitive benefit
Vitamin B12	A reversible cause of cognitive symptoms	200 pg/mL subnormal; if 150-399, check methylmalonic acid
Folate	Can mask B12 anemia, not neurological damage	Serum 3+ ng/mL; RBC 140+ ng/mL
Vitamin D 25-OH	Widely tested, weakly justified	USPSTF I statement; 20 ng/mL adequate
Iron studies / CBC	How B12/folate anemia shows up	No confirmed brain targets; order for fatigue or anemia
Liver and kidney function	Kidney measures feed cardiovascular risk scoring	CKD: eGFR under 60 or albumin-creatinine 30+ for 3 months
Sleep apnea evaluation	Linked to heart disease, diabetes, cognitive impairment	USPSTF I statement if symptom-free; evaluate if snoring/witnessed pauses
Hearing	Largest single midlife factor: relative risk 1.4	USPSTF I statement; screen every 3 years after 50
Vision	Untreated vision loss: relative risk 1.5	USPSTF I statement for acuity screening at 65
Depression screening	Relative risk 2.2, and a common mimic	USPSTF Grade B for all adults; PHQ-9 sensitivity/specificity 0.85

Medication review	Anticholinergic exposure is linked to dementia	Yearly review against Beers Criteria
Cardiovascular risk calculation	Ties every number above into one estimate	AHA PREVENT covers ages 30-79; 10-year risk 7.5%+ lowers treatment threshold

Table B: Optional, Specialized, or Experimental Testing

Only three items below are solidly validated — plasma p-tau217, amyloid or tau PET, and spinal-fluid biomarkers — and only in people who already have symptoms.

Test	Validated or speculative?
CGM (continuous glucose monitor) in non-diabetics	Speculative. Shows promise for personalizing lifestyle interventions, but impact on hard endpoints remains limited; no dementia evidence
Advanced lipid / particle panels	Only ApoB and Lp(a) have guideline standing as selective risk enhancers; NMR particle panels lack endorsement
Broad micronutrient panels	Speculative. Only B12, folate, vitamin D, and blood-count deficiencies have defined thresholds
IgG food-sensitivity panels	Recommended against — has never been scientifically proven to accomplish what it reports to do
Urine mycotoxin panels	Speculative; no society position or validation data confirmed
Provoked heavy-metal testing	Recommended against — not scientifically validated, no demonstrated benefit, may be harmful
Urinary organic acids	Speculative; no validation evidence confirmed
Consumer microbiome / stool tests	Discouraged by international consensus (80.4% agreement); insufficient evidence for routine use
Salivary hormone panels	Speculative; no validation evidence confirmed
Chronic-infection panels	Speculative; no validation evidence confirmed
Whole-body MRI	Not recommended for symptom-free people; no sufficient evidence to justify total-body screening
Brain MRI volumetrics (consumer)	Speculative when sold to symptom-free consumers; interpretation not confirmed outside a memory-clinic workup

Amyloid PET / tau PET	Validated, but not without symptoms — 2025 criteria call it inappropriate for people without cognitive impairment, even APOE4 carriers
CSF (spinal fluid) testing	Validated as a confirmatory reference standard, only within a symptomatic workup
Consumer p-tau217 blood tests	Validated only in symptomatic adults 55+ in specialist settings; FDA says not intended as a screening or stand-alone test. Direct-to-consumer prices run \$200-\$799
Baseline cognitive testing (MoCA, MMSE)	USPSTF I statement if symptom-free; predictive value about 20% at ages 65-74

USPSTF "I" statements recur throughout this table — thyroid, vitamin D, sleep apnea, hearing, vision, cognitive screening. Read them as "we do not know," not "this is bad."

APOE Testing: A Decision Only You Can Make

This guide will not push you toward genetic testing or away from it — only lay out the numbers and trade-offs.

The APOE gene makes a protein that carries cholesterol and other fats. You inherit two copies, giving six combinations: 2/2, 2/3, 2/4, 3/3, 3/4, and 4/4. The epsilon-2 variant may provide some protection and later onset if Alzheimer's occurs (roughly 5-10% carry it). Epsilon-3 is the most common and believed neutral. Epsilon-4 raises risk and brings earlier onset — about 15-25% carry one copy and 2-5% carry two, yet some people with an epsilon-4 allele never develop the disease. Between 40% and 65% of people diagnosed with Alzheimer's carry it. Ancestry matters and is usually left out of marketing: testing positive for APOE-e4 may not mean the same thing across all racial and ethnic groups.

The Absolute Numbers

Relative risks sound frightening and are easy to misread. Versus 3/3, the odds ratio for 4/4 is 14.49 and for 3/4 is 3.63. But risk peaks in the 60s and falls after 80 — epsilon-4 shifts when disease appears more than the lifetime total. Absolute lifetime risk by age, sex, and genotype:

Age and sex	4/4	3/4	3/3	2/2 or 2/3
65, male	4.14%	1.03%	0.28%	0.21%
65, female	1.95%	0.57%	0.17%	0.11%
75, male	28.35%	6.96%	1.78%	1.12%
75, female	27.81%	7.03%	1.69%	1.01%
85, male	50.93%	23.22%	7.76%	4.87%
85, female	60.37%	30.09%	10.23%	6.40%

Researchers summarize 4/4 as roughly 30% risk by 75 and over 50% by 85, and argue APOE should be reclassified from "risk factor" to "major gene." Two honest readings: the female 4/4 estimate is higher at 85 but lower at 65, so "women with epsilon-4 are at higher risk" holds only at older ages; and one copy sits far closer to 3/3 than to 4/4, so treating "APOE4-positive" as one category is misleading.

The Limits of Penetrance and What Testing Feels Like

A 2024 multicohort analysis found 4/4 approaches, but does not reach, the certainty of rare inherited forms: at autopsy, 82% had high Alzheimer's pathology and 88% had clinical Alzheimer's dementia. Twelve percent never got a diagnosis, and the sample came from autopsy referrals — for population risk, use the table above.

Clinically, APOE testing is used primarily in research settings and is not routinely used in clinical care. The main randomized trial on disclosure, REVEAL, tested 162 symptom-free adults with an affected parent, randomized to learning their result or not. Anxiety and depression showed no differences between epsilon-4-positive, epsilon-4-negative, and non-disclosure groups at 6 weeks, 6 months, or 12 months. Elsewhere, 61-73% of epsilon-4-negative people felt relieved versus 11-19% of epsilon-4-positive people, and 15-30% of epsilon-4-positive people felt depressed.

The part that matters most: everyone in REVEAL got a 90-minute session on the limitations of APOE testing and the absence of a medical benefit, plus a counselor meeting, and already-anxious people were screened out. The evidence supports "disclosure is safe when counseled," not "safe when bought online." The Alzheimer's Association is direct: anyone considering genetic testing for any reason should receive genetic counseling before a test is ordered and when results are obtained. APOE4 status does not change your prevention plan. No risk-reduction intervention is recommended only for epsilon-4 carriers, and in US POINTER there was no interaction with APOE epsilon-4 (p=0.95) — the program worked the same regardless of genotype. Note also: the product a worried person would most want, long-term care insurance, is generally not covered by genetic non-discrimination protections (GINA) — settling insurance questions before testing is a sensible order of operations.

Section 10: The Evidence Tables — Quick Reference

This consolidated reference pulls the key intervention, purpose, effect, and caution for the major categories covered in this guide into one place for quick lookup.

Table 1: Lifestyle Interventions

Intervention	Purpose	Key risk / caution
Aerobic exercise, 150 min/week	Keep blood flowing to the heart and brain	Injury from doing too much too soon; ask your clinician before starting if previously sedentary
Resistance training, 2+ days/week	Preserve muscle and physical strength	Strains if form is poor; ask your clinician if new to lifting

High-intensity interval training	Sharpen attention and thinking speed	Hard effort; strain or injury before high-intensity work — clinician clearance advised
Balance and mobility training	Stay steady on your feet	Falls while practicing new moves; use a rail or chair if unsteady
Walking and daily step count	Build brain-healthy movement into the day	Foot or joint soreness
Reducing sitting time	Break up long unbroken sitting	None known
Cardiorespiratory fitness (stamina)	Raise how well the body uses oxygen	Overexertion during hard testing; clinician clearance advised
Fall-prevention program	Avoid falls that injure the brain	Minor strains during training
Helmets and head protection	Prevent traumatic brain injury	None known
Sleeping 7-9 hours a night	Give the brain nightly recovery time via the glymphatic clearance system	None known; treat suspected sleep apnea
Hearing and vision correction	Reduce two of the largest single modifiable risk factors	Cost of devices; ACHIEVE trial found benefit mainly in higher-risk subgroups
Cognitive training	Build and maintain trained mental skills	Gains are mostly confined to the trained skill, not general intelligence
Social engagement	Counter isolation, RR 1.6 and 5% weighted PAF	None known
Depression treatment	Address the single highest relative risk factor (2.2)	Requires clinical evaluation

Table 2: Metabolic and Vascular Interventions

Intervention	Purpose	Evidence strength
Systolic blood pressure at or under 130 mm Hg	Reduce small-vessel brain damage	Strong (RCT, Class 1 guideline)
12-hour overnight fast	Improve metabolic flexibility and insulin sensitivity	Strong (controlled trials) for timing; weaker for cognitive outcomes specifically

KetoFLEX 12/3 food pattern	Lower glycemic load, raise fiber and healthy fat	Moderate (overlaps with Mediterranean/MIND evidence)
Weight and waist management	Reduce midlife obesity risk (RR 1.3)	Observational (moderate)
Diabetes screening and control	Address RR 1.7 for dementia	Strong for general health; mixed for dementia-specific drug prevention
LDL and lipid management	Address RR 1.3 for high LDL	Moderate (statins: strong observational, negative in RCTs for dementia specifically)

Table 3: Environmental and Medical Interventions

Intervention	Purpose	Evidence strength
Dental hygiene and periodontal treatment	Reduce inflammation linked to cognitive impairment (OR 1.77)	Moderate observational; no trial proof treatment changes cognition
Bedroom HEPA filtration	Reduce PM2.5 exposure (RR 1.1, 3% weighted PAF)	Weak-moderate for dementia; strong for respiratory health
Tap water testing (older plumbing/wells)	Eliminate lead exposure	Strong for general health; no direct dementia RCT
Limiting high-mercury fish	Avoid neurotoxin exposure	Established general guidance (FDA/EPA)
Adult vaccination (zoster, flu, pneumococcal, Tdap)	Associated with lower dementia risk across large meta-analyses	Moderate-strong observational, including natural experiments
Gut-supportive diet (fiber, fermented foods)	Support gut-brain axis health	Emerging/preliminary

Section 11: Sources and Further Reading

Every link below has been checked and points to the live, canonical page for that source rather than a fragile deep-link that may break.

Source	Link
2024 Lancet Commission on Dementia Prevention, Intervention, and Care	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(24)01296-0/fulltext
WHO Guidelines on Physical Activity and Sedentary Behaviour (2020)	https://www.who.int/publications/i/item/9789240015128
WHO Risk Reduction of Cognitive Decline and Dementia Guidelines	https://www.who.int/publications/i/item/9789241550543
Alzheimer's Association — 10 Healthy Habits for Your Brain	https://www.alz.org/help-support/brain_health/10-healthy-habits-for-your-brain
Alzheimer's Association — Can Alzheimer's Disease Be Prevented?	https://www.alz.org/alzheimers-dementia/research-and-progress/prevention
National Institute on Aging — Could Fasting Reset the Body's Clock?	https://www.nia.nih.gov/news/could-fasting-reset-bodys-clock-and-protect-brain-against-alzheimers
National Institute on Aging — Gut Microbiome and Alzheimer's	https://www.nia.nih.gov/news/beyond-brain-gut-microbiome-and-alzheimers-disease
National Institute on Aging — Loneliness Linked to Dementia Risk	https://www.nia.nih.gov/news/loneliness-linked-dementia-risk-large-scale-analysis
Alzheimers.gov — Changes in Human Microbiome Precede Cognitive Decline	https://www.alzheimers.gov/news/changes-human-microbiome-precede-alzheimers-cognitive-declines
US Preventive Services Task Force — Recommendations	https://www.uspreventiveservicestaskforce.org/uspstf/
American Heart Association — Life's Essential 8	https://www.heart.org/en/healthy-living/healthy-lifestyle/lifes-essential-8
PMC — Sleep and Beta-Amyloid Clearance (PMC4323377)	https://pmc.ncbi.nlm.nih.gov/articles/PMC4323377/
PMC — Nutrient Deficiencies and Dementia Incidence (PMC11247665)	https://pmc.ncbi.nlm.nih.gov/articles/PMC11247665/
PMC — Ketogenic Approaches Review (PMC7642953)	https://pmc.ncbi.nlm.nih.gov/articles/PMC7642953/
PMC — Cognitive Training Review (PMC5991350)	https://pmc.ncbi.nlm.nih.gov/articles/PMC5991350/

PMC — Vascular Risk Factors Review (PMC7272467)	https://pmc.ncbi.nlm.nih.gov/articles/PMC7272467/
PMC — Additional Dementia Risk Review (PMC7483955)	https://pmc.ncbi.nlm.nih.gov/articles/PMC7483955/
PMC — Metformin Time-Related Bias Review (PMC9484147)	https://pmc.ncbi.nlm.nih.gov/articles/PMC9484147/
PMC — SELECT Trial Post-Hoc Analysis (PMC13452022)	https://pmc.ncbi.nlm.nih.gov/articles/PMC13452022/
PMC — Statin Cognitive Meta-Analysis (PMC4351273)	https://pmc.ncbi.nlm.nih.gov/articles/PMC4351273/
PMC — APOE Penetrance Multicohort Study (PMC11736423)	https://pmc.ncbi.nlm.nih.gov/articles/PMC11736423/
PMC — Aspirin ASPREE Trial (PMC7455352)	https://pmc.ncbi.nlm.nih.gov/articles/PMC7455352/
PMC — Organophosphate Cohort Study (PMC5798900)	https://pmc.ncbi.nlm.nih.gov/articles/PMC5798900/

Source	Link
Stanford Medicine — Estrogen-Based Hormone Therapy and Alzheimer's Risk	https://med.stanford.edu/news/all-news/2026/08/study-ties-estrogen-based-menopausal-hormone-therapy-to-lower-al.html
ScienceDirect — Ketogenic Diet Trial Data	https://www.sciencedirect.com/science/article/pii/S2352873718300490
PubMed — Cognitive Decline Study (PMID 31241312)	https://pubmed.ncbi.nlm.nih.gov/31241312/
PubMed — Chlamydia Pneumoniae Review (PMID 31626972)	https://pubmed.ncbi.nlm.nih.gov/31626972/
Nutrition Insight — Fasting and Time-Restricted Diets, Dementia Risk	https://www.nutritioninsight.com/news/fasting-time-restricted-diets-dementia-brain-health.html
News-Medical — Time-Restricted Eating and Dementia Risk in Older Women	https://www.news-medical.net/news/20260726/Time-restricted-eating-may-help-lower-dementia-risk-in-older-women.aspx
Alzheimer's Drug Discovery Foundation — Intermittent Fasting and Dementia	https://www.alzdiscovery.org/cognitive-vitality/blog/can-intermittent-fasting-help-prevent-dementia
Journal of Nutrition — Protein Intake and Aging (fulltext)	https://jn.nutrition.org/article/S0022-3166(24)00289-X/fulltext
Hopkins Medicine — Dementia Overview	https://www.hopkinsmedicine.org/health/conditions-and-diseases/dementia

Hopkins Medicine — Alzheimer's Disease Overview	https://www.hopkinsmedicine.org/health/conditions-and-diseases/alzheimers-disease
Alzheimer's & Dementia: Translational Research & Clinical Interventions — DOI 10.1002/trc2.70197	https://doi.org/10.1002/trc2.70197
University of Cambridge — Why More Education Lowers Dementia Risk	https://www.cam.ac.uk/research/news/why-more-education-lowers-dementia-risk
PubMed — Gut Microbiome and Alzheimer's Study (PMID 39201303)	https://pubmed.ncbi.nlm.nih.gov/39201303/
PubMed — Study PMID 41269248	https://pubmed.ncbi.nlm.nih.gov/41269248/
PubMed — Study PMID 38577491	https://pubmed.ncbi.nlm.nih.gov/38577491/
US EPA — Lead in Drinking Water	https://www.epa.gov/ground-water-and-drinking-water/basic-information-about-lead-drinking-water
FDA/EPA — Fish Advice for Mercury	https://www.fda.gov/food/consumers/questions-answers-fish-and-mercury
2023 AGS Beers Criteria (American Geriatrics Society)	https://www.americangeriatrics.org/press-releases/updated-ags-beers-criteria-2023
NIA — Genetics Fact Sheet on APOE	https://www.nia.nih.gov/health/alzheimers-causes-and-risk-factors/alzheimers-disease-genetics-fact-sheet
NEJM — REVEAL Study on APOE Disclosure	https://www.nejm.org/doi/full/10.1056/NEJMoa0806906
Alzheimer's Association — alz.org (home)	https://www.alz.org

All links were verified as live and pointing to their canonical source page at the time this guide was produced. Government and .gov domains (NIA, alzheimers.gov, EPA, FDA), academic institutions, and major journal/publisher domains (Lancet, PMC, PubMed, NEJM) are the most stable long-term; news-site links may be reorganized over time.