Supplementary Data

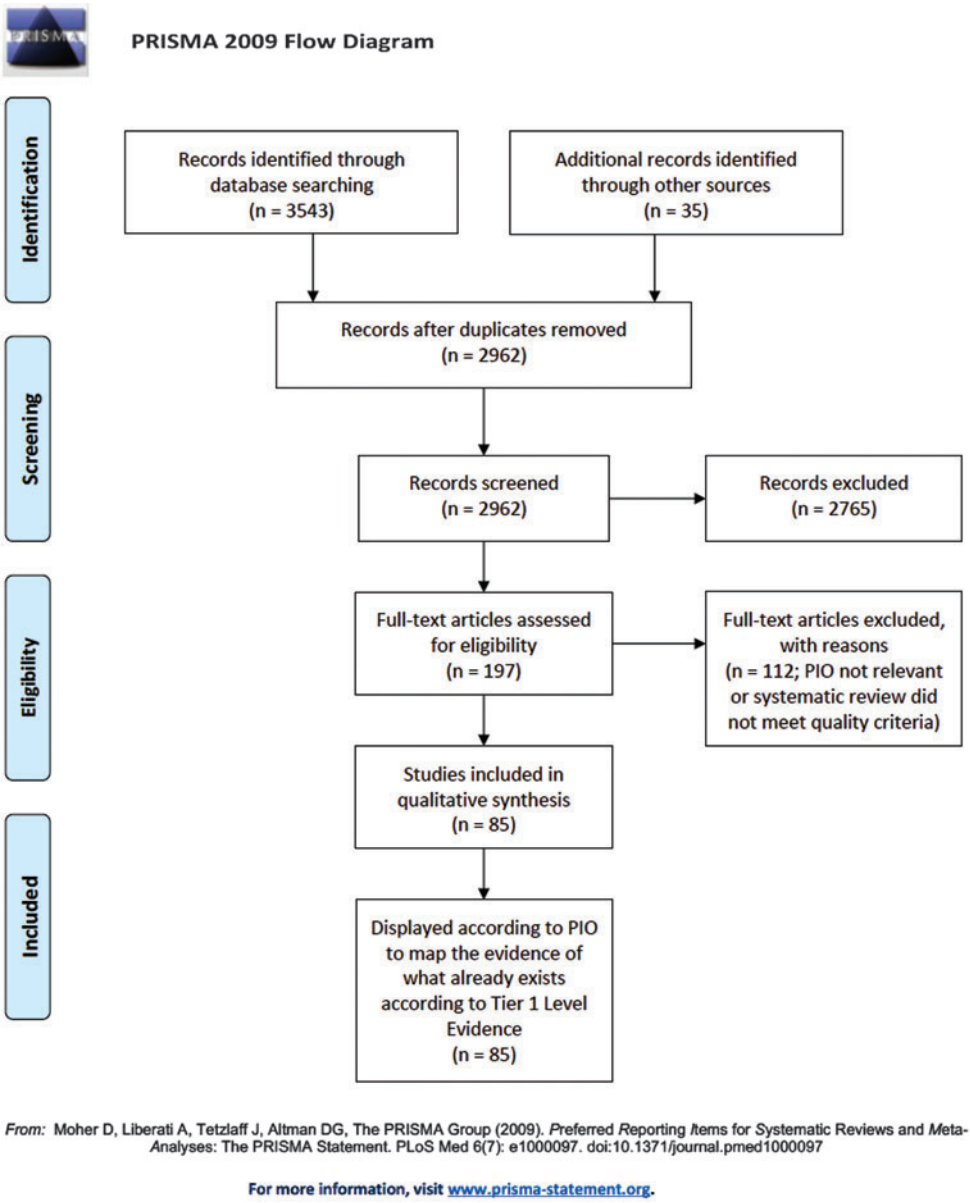
Supplementary Data S1. Umbrella Review and Evidence Mapping Exercise to Identify Systematic Review/Meta-analyses: What Already Exists in Terms of Evidence?

PubMed and Cochrane database for systematic reviews (Cochrane Dementia and Cognitive Improvement Group) databases were searched to determine the breadth of systematic review and meta-analysis literature for each of the 72 ingredients yielded from the scoping review. Searches were conducted throughout the week of 15APR19. Publications from 1993 to 2019 related to dietary supplements and cognitive performance located on the U.S. Army Research Institute of Environmental Medicine website under Military Nutrition were also reviewed.

Two reviewers screened the titles/abstracts yielded from the searches for initial eligibility based on predefined eligibility criteria (Supplementary Table S1). Full-text articles of relevant citations were examined for methodological

SUPPLEMENTARY TABLE S1. ELIGIBILITY CRITERIA FOR *BROAD* STRATEGY TO IDENTIFY WHAT ALREADY EXISTS FROM SYSTEMATIC REVIEWS: *ARE THERE SPECIFIC DIETARY INGREDIENTS THAT CAN SAFELY BE USED TO EFFECTIVELY ENHANCE BRAIN HEALTH/COGNITIVE PERFORMANCE-RELATED OUTCOMES?*

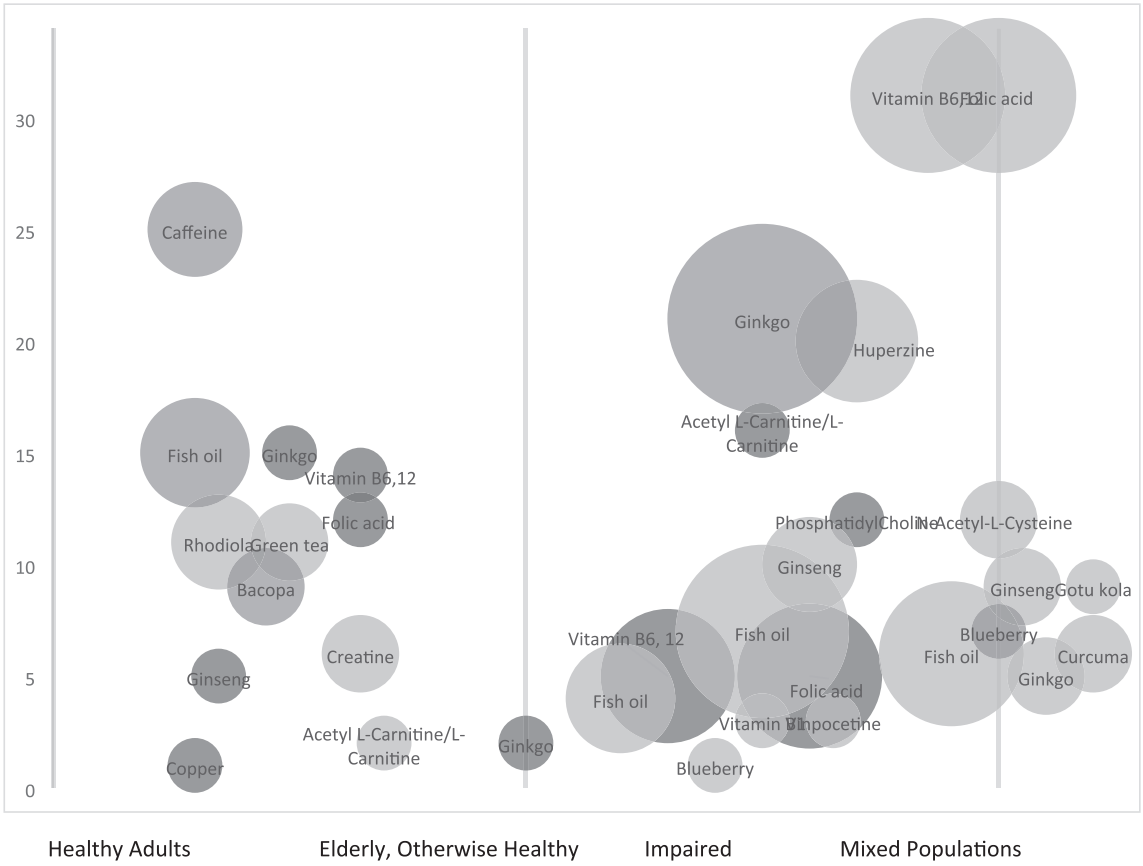
Eligibility criteria	*Broad eligibility used to examine ''what exists''*	*Search strategy*
Population	Any adults (18+ years old), healthy or unhealthy, with any cognitive impairment, including mild cognitive impairment or Alzheimer's disease, with or without dementia.	No initial restrictions to learn ''what exists.''
Intervention	Any dietary supplement/ingredient defined as any product that met the following criteria: (a) any product (other than tobacco) intended to supplement the diet that contains one or more of the following ingredients: a vitamin, mineral, herb or other botanical, an amino acid, a concentrate, metabolite, constituent, extract, or combination of any of these ingredients; (b) administered in any form (e.g., tablet, capsule, soft gel, gel cap, liquid, powder, gel, chews, inhalant, nasal spray, skin patches/lotions/applications); (c) not represented as conventional food or as a sole item of a meal or of the diet (e.g., sport drinks, shakes, bars); (d) included a ''Supplement Facts'' rather than ''Nutrition Facts'' panel.[S1,S2]	Seventy-two prevalent dietary ingredients across products identified. Specific ingredient names coupled with their scientific names and common names were used to create search string. *Studies were only eligible if they examined the ingredient as an intervention; studies on dietary intake/status or association between levels and disease progression were excluded.*
Control/Comparator(s)	Sham (placebo), no treatment and/or active comparators.	No restrictions; comparators will be later grouped according to type.
Outcome(s)	Brain health and cognitive performance-related outcomes, e.g., brain function, memory, alertness, concentration, mental health, focus, clarity, recall, energy, cognition, cognitive performance, mental performance, mental decline, cognitive function, brain health.	The authors executed the following search, which includes MeSH strategy, to capture all outcomes: *(mental processes OR cognitive dysfunction OR ''brain health'' OR ''cognitive health'' OR mental health OR ''brain function'' OR ''cognitive function'' OR executive function OR ''mental clarity'' OR ''cognitive ability'' OR ''cognitive performance'' OR ''mental performance'' OR ''reaction time OR memory OR problem-solving OR ''energy'' OR ''alert'' OR ''focus'' OR attention OR concentration)*
Study Design(s)	The authors will look for evidence first through quality systematic reviews and meta-analyses; if no evidence exists, they will then look for randomized clinical trials; *published protocols and previously updated reviews are excluded.*	Search limiters used to target systematic reviews/meta-analyses before moving into other study designs.
Timing	The authors are interested both in acute and long-term use and performance, initially.	No restrictions; later to categorize into different categories of timing.



SUPPLEMENTARY FIG. S1. Flow chart.

quality (e.g., a transparent search strategy, quality assessment of included studies, and defined eligibility criteria; narrative reviews/expert opinions and studies only examining levels of an ingredient within the body were excluded).

Supplementary Figure S1 displays the flow of citations. Of the 3,578 citations retrieved from the various searches, 616 citations were excluded as duplicates, 2877 were ineligible (Supplementary Table S1), and 85 systematic review studies met the broad eligibility criteria (Supplementary Table S2). The extent of the systematic review/meta-analysis literature is graphically mapped in Supplementary Figure S2. The evidence of effectiveness across outcomes is not presented here (forthcoming in another article that includes other study designs and informs evidence-based decision-making). The purpose of this report is simply to describe where gaps are in the published, relevant literature.



SUPPLEMENTARY FIG. S2. Evidence map of systematic reviews/meta-analyses. *X*-axis is the types of populations studied (left to right: healthy adults, elderly otherwise healthy, impaired, mixed populations). *Y*-axis: number of RCTs in largest systematic review/meta-analysis. Bubble size is the number of quality systematic reviews published to date. RCT, randomized controlled trials.

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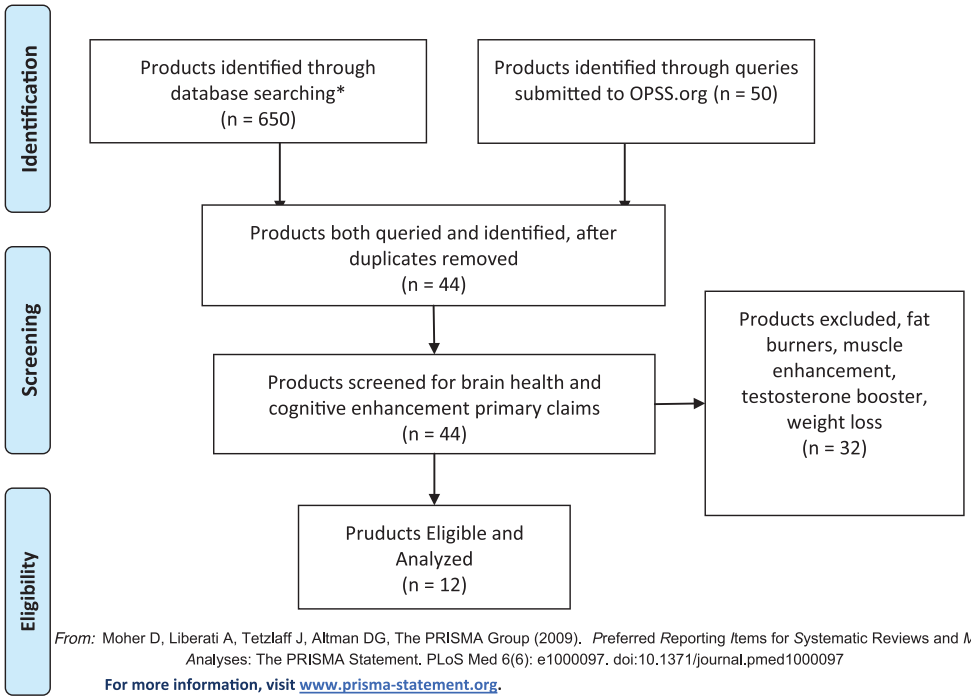
SUPPLEMENTARY DATA S2. PRODUCT SELECTION FLOW CHART

Database searched[a]	*Search strategy*	*No. of products retrieved*	*Total unique products*
Dietary Supplement Label Database	Advanced search: label claims must include ''brain'' and must include ''performance''	170	468
	Advanced search: products with ''cognitive function'' in claims	250	
	Advanced search: product names with ''brain''	183	
GNC website	Dietary supplements to support ''brain and memory health''	21	12
Natural medicines	Commercial products: ''brain''		170
	Herbs, foods, and supplements: people use this for: ''cognitive''	261	
	Herbs, foods, and supplements: people use this for: ''brain''	14	
Amazon.com	Supplement and brain	Used as cross-check with above searches	
Shopmyexchange.com	Supplement and cognitive		



Supplementary Data S3. Instrumentation and Analytic Conditions

Liquid chromatography-quadrupole time-of-flight mass spectrometry

The liquid chromatographic system was an Agilent Series 1290 comprising the following modular components: binary pump, an autosampler with 100-well tray, and a thermostatically controlled column compartment. Separation was achieved on an Agilent Poroshell 120 EC C18 (2.1×150 mm, 2.7 μ) column at a flow rate of 0.2 mL/min. The mobile phase consisted of water with 0.1% formic acid (A) and acetonitrile with 0.1% formic acid (B) using the following gradient elution: 0 min, 99% A: 1% B, isocratic for next 3 min, then for next 27 min 55% A:45% B, then to 100% B in next 20 min. Each run was followed by a 3-min wash with 100% B and an equilibration period of 5 min with 99% A/1% B. Two microliters of sample was injected and column temperature was maintained at 35°C. The mass spectrometric analysis was performed with a quadrupole time-of-flight-Mass Spectrometry (Model no. G6530A; Agilent Technologies, Palo Alto, CA) equipped with an electrospray ionization source with Jet Stream technology using the following parameters: drying gas (N_2) flow rate, 7.0 L/min; drying gas temperature, 300°C; nebulizer, 25 psig, sheath gas temperature, 300°C; sheath gas flow, 7 L/min; capillary, 3500 V; skimmer, 65 V; fragmentor voltage, 100 V. The sample collision energy was set at 35 eV. All the operations, acquisition, and analysis of data were

controlled by Agilent MassHunter Acquisition software ver. A.05.00 and processed with MassHunter Qualitative Analysis software ver. B.08.00. Each sample was analyzed in both positive and negative modes in the range of m/z = 50–2500. Accurate mass measurements were obtained by means of ion correction techniques using reference masses at m/z 121.0509 (protonated purine) and 922.0098 [protonated hexakis (1H, 1H, 3H-tetrafluoropropoxy) phosphazine or HP-921] in positive ion mode, while at m/z 112.9856 (deprotonated trifluoroacetic acid-[TFA]) and 1033.9881 (TFA adducted HP-921) were used in negative ion mode. The compounds were confirmed in each spectrum using accurate mass. For this purpose, the reference solution was introduced into the ESI source via a T-junction using an Agilent Series 1200 isocratic pump (Agilent Technologies, Santa Clara, CA) using a 100:1 splitter set at a flow rate of 20 μL/min. Only single tests were run for each of the select products.