

Review of Dairy Consumption and Cognitive Performance in Adults: Findings and Methodological Issues

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Key Words

Dairy food intake · Cognitive functioning · Methodological review

Abstract

Background: Diet is a modifiable factor that could be targeted as an appropriate intervention to optimise cognitive health and well-being in ageing. **Aim:** The aim of this systematic review was to consider current evidence for an association between dairy intake and cognitive functioning. **Methods:** Searches of the electronic databases Medline, Embase, Web of Science, CINAHL, and PsychInfo were undertaken to identify peer-reviewed journal articles that reported on associations between dairy consumption and cognitive outcomes. **Results:** Three cross-sectional and 5 prospective studies were identified. Poorer cognitive function and an increased risk for vascular dementia were found to be associated with a lower consumption of milk or dairy products. However, the consumption of whole-fat dairy products may be associated with cognitive decline in the elderly. **Conclusion:** Methodological variability and study limitations do not enable conclusions regarding optimal dairy intake and cognitive performance to be drawn. Randomised controlled trials are needed to confirm the relationship between dairy intake and cognition.

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Introduction

As the populations of developed nations around the world age [1], cognitive decline and dementia are emerging as major health problems. Cognitive decline may range from the very minimal decline that is associated with normal ageing, to mild cognitive impairment (MCI), or very severe dementia, with the latter regarded as the clinical end-point of cognitive impairment [2]. The worldwide prevalence of dementia is increasing and is predicted to affect 81.1 million people by 2040 [3], placing a considerable burden on health care resources, and impacting substantially on the quality of life of the individuals afflicted and their families. As the precise aetiology of cognitive decline is not known, and there is no cure, interventions that may slow or prevent this condition have become a health priority.

There is a substantial body of evidence indicating that nutrition may play an important role in the causation and prevention of age-related cognitive decline and dementia [4, 5]. While positive associations have been shown between a number of nutrients and cognitive performance, including antioxidants, folate, omega-3 and omega-6 fatty acids, little attention has been paid to the potential role of dairy foods in modulating psychological parameters. This is despite recent epidemiological, observational and intervention studies providing evidence for the role of dairy in

improving cardiovascular risk factors and lowering the prevalence of metabolic syndrome. Dairy consumption may reduce the likelihood of cognitive decline either directly, or via mediating effects on cardiometabolic health.

The primary objective of this review was to identify published literature which has reported associations between dairy consumption and cognitive performance in order to identify whether there is any evidence for a beneficial effect of dairy consumption on cognition.

Methods

Search Strategy

A search was undertaken on Medline (1950 to July 2009), Web of Science (1968 to July 2009), Embase (1980 to July 2009), CINAHL (1981 to July 2009), and PsychInfo (1800s to July 2009) for studies that reported an association between dairy intake (or intake of individual dairy products) and cognitive function or psychological health. The search terms used were *dairy, milk, cheese, yogurt* as isolated words and in combination with *food, intake, consumption, and cognition, cognitive decline, cognitive performance, cognitive impairment, cognitive function/dysfunction, cognitive state, dementia, Alzheimer's disease, mild cognitive impairment, depression, mental illness, psychological/mental health*. In addition to electronic database searches, additional papers were retrieved by reviewing reference lists of all studies identified in the initial electronic search. Letters, conference proceedings, abstracts of dissertations and reviews were not included but were screened for additional references that met the inclusion criteria.

Inclusion and Exclusion Criteria

Included papers were limited to studies involving adults only, and written in English language, unless a translation of a non-English paper was readily available. Only studies with a quantitative assessment of dairy food intake were included, i.e. studies which reported a total measure of dairy intake from a number of different dairy products, or studies which measured individual consumption of specific dairy products, such as milk and cheese. Papers deemed eligible for inclusion also had to report at least 1 measure of cognitive function or cognitive status, including the presence or absence of dementia, Alzheimer's disease (AD) or MCI.

Data Extraction and Methodological Appraisal

Pre-determined information provided in each paper was extracted in order to be summarised for comparison. This included details about the study design (cross-sectional or prospective), the location of the study, and participant characteristics (number, gender and age at baseline and/or follow-up of subjects). Any exclusion criteria were summarised. Detailed information about the measure of cognitive function used was extracted from each paper, including what was assessed (e.g. dementia), how the outcome measure was assessed (e.g. specific questionnaire or clinical criteria), and the definition used to define impairment (e.g. cut-off score or clinical diagnosis). Details provided regarding dairy intake were also extracted. This information included the measure used to quantify dairy intake (e.g. diet recall, food questionnaire), the specific dairy foods measured (e.g. milk, cheese), the serving

size of dairy used in analyses, and the fat content of the dairy measured. Details about the study findings included the type of statistical analyses performed, such as adjustments made, the proportion of subjects defined as having cognitive or psychological impairment, and the main findings in regard to a quantity of dairy intake associated with cognitive or psychological function.

The included studies were scored on their methodological quality on the basis of a modified checklist (table 1) developed for observational longitudinal studies [6], and entailed the 6 areas of potential study bias recommended to be included in any quality appraisal component of systematic reviews [7]. Criteria were adapted to allow appraisal of both cross-sectional and longitudinal studies and assessed methodological quality in 6 areas: (1) study participation, (2) study attrition, (3) measurement of predictor variable, (4) measurement of outcome variable, (5) confounding measurement, and (6) analysis. Each criterion was scored as yes (1), no (0), or partly (1/2) based on information provided in the paper, and a total score out of 20 was calculated (see Appendix).

The primary author (G.E.C.) was responsible for all literature searches, assessed the eligibility of each paper, performed all data extraction and conducted the methodological appraisal and scoring. A formal meta-analysis was not performed because of the limited number of studies, the heterogeneity of study design and assessment of both dairy and cognitive (or psychological) functioning, differences in adjustment for confounding, and statistical analyses used to present results.

Results

Results of the Search

The literature search yielded a total of 216 citations. After removing duplicates, 132 papers remained. The titles and abstracts of these papers were screened to identify potentially relevant papers for full review. The full text was obtained for 30 papers deemed to be potentially relevant. Eight papers were excluded because they did not include specific measures of cognition, 5 papers examined soy, a milk probiotic or vitamin D and not dairy, 3 papers reported on the influence of food diversity (rather than dairy) on cognition, 3 papers examined dietary intake in schizophrenic populations, 2 papers only reported on associations between dairy intake and survival risk or mortality, and 1 paper was a review.

Based on the selection criteria, 8 papers from 7 different studies were included in this review. Two of the included papers both reported on the Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) study [8, 9] but have been treated as separate studies for the purpose of this review. The papers examined different outcome measures, namely, different aspects of cognition. Eskelinen et al. [8] examined actual cognitive performance as measured by neuropsychological tests, in addition to MCI. An important differentiation is that this paper excluded participants

Table 1. Checklist for methodological assessment of cross-sectional and longitudinal studies included in the review

<i>Study participation</i>	
(1) The population of interest adequately described in terms of key characteristics, and represented by sample	
(2) Sampling, recruitment methods, time and place of recruitment adequately described	
(3) Inclusion and exclusion criteria adequately described	
(4) Baseline characteristics of study sample adequately described (number of participants, age, gender, health status)	
<i>Study attrition</i>	
Cross-sectional design	Longitudinal design
(5) Justification or explanation for the number of participants	(5) Specification of numbers at each follow-up period and duration of follow-up
(6) Explanation of how missing data was dealt with	(6) Analyses conducted to determine whether participants lost to follow-up do not significantly differ in key characteristics/outcomes from those who completed the study
<i>Measurement of predictor variable</i>	
(7) Method used to assess dietary intake adequately described and reference provided	
(8) Reliability and validity of measurement tool(s) mentioned	
(9) Mean dairy intake adequately described in sample (including type, quantity)	
(10) Type of dairy associated with outcome measure of interest clearly described (product and fat content)	
(11) Quantity of dairy associated with outcome measure of interest clearly described (number of servings and specified serving size, or amount in g/ml per day)	
<i>Measurement of outcome variable</i>	
(12) Method used to assess cognition adequately described	
(13) Cognition measure included that is not a screening tool	
(14) Criteria used to diagnose impairment provided (or definition of cognitive impairment provided if not from diagnosis)	
(15) Number of participants with cognitive impairment provided (at baseline and/or follow-up)	
<i>Confounding measurement</i>	
(16) Potential confounders mentioned and accounted for in analyses	
<i>Analysis</i>	
(17) Specific type of analyses adequately described	
(18) Measure of association provided with confidence intervals	
(19) Effect sizes reported	
(20) The impact of biases/limitations to study assessed qualitatively	
Criteria: rated as 1 (yes), 0 (no), 1/2 (partly).	

with dementia at the follow-up examination. Laitinen et al. [9] included those with dementia, as dementia and AD were the primary outcome measures. For these reasons, the 2 papers have been added as 2 studies.

Summary of Included Studies

The included studies consisted of 3 cross-sectional [10–12] and 5 prospective studies [8, 9, 13–15]. The follow-up duration of the prospective studies ranged from 3.3 [13] to 30 years [15]. There were no randomised controlled trials identified in the literature that manipulated dairy intake and assessed any changes in cognitive function. Table 2 describes the study design, cohort, location, number and ages of participants, and the exclusion criteria for the studies included in this review, grouped by study design

and listed by quality appraisal score in descending order. The predictor and outcome measures used are detailed in table 3, and the main findings of each study are presented in table 4. All 8 papers were published after the year 2000. Studies were conducted in America (1 in the United States, 1 in Mexico), Europe (1 in France, 2 in Finland), Australia (1), and Asia (1 in Korea, 1 in Japan).

Participants

One study included only males [13], 1 study included only females [14] and the remaining 6 included both genders [8–12, 15]. Sample sizes ranged from 449 [11] to 4,809 [14]. The majority of studies included middle-aged to elderly populations. In the 3 cross-sectional studies, there were no participants under the age of 40 years. Follow-up

Table 2. Characteristics of studies reporting associations between dairy consumption and cognition

Study	Cohort, FUD (prospective studies)	Country	Age, mean or range, years	Number		Exclusion criteria	Adjustments	Quality score, /20
				M	F			
Cross-sectional								
Lee et al. [11]	Korean elderly	Korea	60–83	210	239	Major cognitive impairment	Age	8.0
Avila-Funes et al. [10]	Study on Health, Welfare and Aging	Mexico	64.4	465	1,283	Nil specified	Nil	9.5
Rahman et al. [12]	Survey of Alabama’s Elderly	USA	55–94	345	711	Nil specified	Age, race, gender, education, dietary factors	11.5
Prospective								
Almeida et al. [13]	Australian elderly men FUD: 3.3–6.8 years	Australia	Baseline: ≥75 Follow-up: ≥80	601		Nil specified	Analyses repeated excluding subjects with AD, dementia/memory problems, depression	10.5
Laitinen et al. [9]	CAIDE study FUD: 21 years	Finland	Baseline: 50.4 Follow-up: 71.3	549	900	Nil specified	Age, gender, education, FUD, other fat subtypes from milk products, ApoE4 status, vascular risk factors, history of vascular disorders	11.5
Yamada et al. [15]	Adult Health Study, atomic bomb survivors FUD: 25–30 years	Japan	Baseline: 35–60 Follow-up: 60–90	475	1,299	Nil specified	Age, sex, education	11.5
Eskelinen et al. [8]	CAIDE Study FUD: 21 years	Finland	Baseline: 50.2 Follow-up: 71.1	506	835	Dementia at follow-up	Age, gender, education, FUD, other fat subtypes from milk products, ApoE4 status, midlife vascular risk factors	12.5
Vercambre et al. [14]	Cohort from the Epidemiological Study of Women of MGEn Study FUD: 13 years	France	Baseline: 62–68 Follow-up: 76–82		4,809	Energy intake deemed non- plausible	Age, education, physical activity, energy intake, smoking, supplement consumption, use of postmenopausal hormones, diabetes, hypertension, hypercholesterolaemia, CHD, stroke, cancer, depression	16.0

FUD = Follow-up duration; MGEN = Mutuelle Generale de l'Education Nationale. Quality score was calculated on 20 criteria based on the reporting of the study design and method, study attrition, measurement of dairy intake, assessment of cognition, and statistical analysis.

assessments in all prospective studies were conducted in individuals over the age of 60. Studies recruited elderly people possibly representative of the population in that region [10, 12, 13], used subsamples of subjects from larger health studies [8, 9, 14], recruited atomic bomb survivors [15], and elderly people from a welfare centre [11]. Two of the 9 studies excluded those with major cognitive impairment [11] or dementia at follow-up [8].

Assessment of Cognitive Functioning

A variety of assessment procedures were used to measure cognitive status. Six out of the 8 studies used a dementia screening tool, either the Mini-Mental State Examination or the Mental Status Questionnaire as a measure of cognitive function. For 4 studies, this was the sole measure to determine cognitive function [10–13]. The 2 CAIDE studies [8, 9] used the Mini-Mental State Examination in addition to standardised dementia, AD or MCI diagnostic criteria. One study applied a number of dementia screen-

ing instruments in conjunction with diagnostic criteria [15]. An indirect measure of cognitive function was utilized by Vercambre et al. [14], who sent a cognitive deterioration scale to a close relative or friend of each participant. The informant was required to complete the scale by evaluating any observed cognitive deterioration over the past year. Two studies assessed depression using the Geriatric Depression Scale in addition to cognitive state [10, 13].

Assessment of Dairy Intake

One cross-sectional and 5 prospective studies applied a food frequency questionnaire or self-reported questionnaire including dietary measures to assess dairy intake [8–10, 13–15]. The remaining cross-sectional studies used a 24-hour diet recall [11] and a home interview [12].

Main Findings

Two cross-sectional studies [11, 12] and 1 out of the 5 prospective studies [15] reported a beneficial effect from

Table 3. Outcome measures of studies reporting associations between dairy consumption and cognition

Study	Outcome measure: cognition function		Predictor: dairy intake measures			
	domain assessed	tool/criteria used	definition of impairment	measure used	individual dairy foods specified	serving size defined
Cross-sectional						
Lee et al. [11]	Dementia screening	MMSE-K-12	Impaired cognitive function: MMSE-K ≤ 19 Inadequate cognitive function: MMSE-K 19–23	Interview: 24 h diet recall	No	No
Avila-Funes et al. [10]	Dementia screening (depression)	Abbreviated MMSE GDS-15	Impaired cognitive function: MMSE ≤ 12 Depression: GDS-15 ≥ 6	Mini-Nutritional Assessment questionnaire	No	No
Rahman et al. [12]	Dementia screening	MSQ	Impaired cognitive function: MSQ < 9	Home interview	Milk, cheese	No
Prospective						
Almeida et al. [13]	At follow-up: Dementia screening Depression	MMSE GDS-15	'Preserved cognitive function': MMSE ≥ 24 'Preserved mood': GDS ≤ 5 'Successful mental health aging': MMSE ≥ 24 and GDS ≤ 5	At baseline: self-report questionnaire, including diet measures	Full-cream milk	No
Laitinen et al. [9]	At follow-up: Dementia screening Clinical dementia	MMSE Clinical diagnosis: DSM-IV criteria	Clinical diagnosis of dementia or AD	At baseline: FFQ	Milk, sour milk, spreads	No
Yamada et al. [15]	At follow-up: Clinical dementia:	CASI IQCODE (by the caregiver) Hachinski's Ischemic Score Clinical Dementia Rating Clinical diagnosis: DSM-IV criteria	Clinical diagnosis of dementia	At baseline: FFQ: milk	Milk	No
Eskelinen et al. [8]	At follow-up: Dementia screening Clinical MCI Episodic memory Semantic memory Psychomotor speed Executive function Prospective memory	MMSE Mayo Clinic AD Research Centre criteria Word recall tests Category Fluency test Purdue Peg Board task Letter digit substitution test Stroop test Einstein task	Clinical diagnosis of MCI	At baseline: FFQ	Milk, sour milk, spreads	No
Vercambre et al. [14]	At follow-up: Recent cognitive decline	DECO scale (by close relative or friend)	'Recent cognitive decline': DECO < 33	At baseline: diet history questionnaire	Milk and yogurt, cheese, dairy desserts and ice cream	No

CASI = Cognitive Ability Screening Instrument; DECO = Observed Cognitive Deterioration scale; FFQ = food frequency questionnaire; GDS = Geriatric Depression Scale; IQCODE = Informative Questionnaire on Cognitive Decline in the Elderly; MMSE = Mini-Mental State Examination; MMSE-K = Mini-Mental State Examination for Koreans; MSQ = Mental Status Questionnaire.

Table 4. Main findings of studies reporting associations between dairy consumption and cognition

Study	Statistical analyses	Percentage with impairment	Range of dairy intake	Main findings with regard to dairy and cognitive function	Secondary findings
Cross-sectional					
Lee et al. [11]	ANOVA	Cognitive function: Poor: 22.3% Inadequate 28.3%	Milk and dairy products: absolute amount	Women with poor cognitive function had significantly lower intakes of milk and dairy products, $p < 0.05$, than those with inadequate or normal cognitive function No significant differences for men	
Avila-Funes et al. [10]	Linear regression	Cognitive impairment: 8.2% (Depressive symptoms: 66%)	Not specified	No reported association between cognitive impairment and milk product consumption	Consumption of milk products significantly lower in those with depressive symptoms ($p < 0.01$)
Rahman et al. [12]	Logistic regression	Cognitive impairment: 16.6%	Cheese and milk: <1 serving/week or never to >1 serving/week	Higher cheese intake associated with reduced likelihood of cognitive impairment (OR = 0.68, 95% CI = 0.47–0.99) Milk intake not associated with cognitive impairment	Dose-response effect; as cheese intake increased, risk of cognitive impairment decreased ($p < 0.01$)
Prospective					
Almeida et al. [13]	Cox proportional hazards regression	Impaired cognitive function: 17.6% (Impaired mood: 8.8% Poor mental health: 24%)	Full-cream milk: 'regular consumption' (quantity not specified)	Consumption of full-cream milk associated with impaired cognitive function (OR = 0.59, 95% CI = 0.37–0.94)	Consumption of full-cream milk associated with poor mental health (OR = 0.57, 95% CI = 0.37–0.86)
Laitinen et al. [9]	Logistic regression	Clinical dementia: 4.2%	Fat intake from milk products and spreads, g	Fat intake from milk products (milk and sour milk) not significantly associated with risk of dementia or AD Moderate intakes of PUFA from spreads associated with decreased risk of dementia (OR = 0.40, 95% CI = 0.17–0.94) Moderate intakes of SFA from spreads associated with increased risk of dementia (OR = 2.45, 95% CI = 1.10–5.47) and AD (OR = 3.82, 95% CI = 1.48–9.87)	
Yamada et al. [15]	Logistic regression	Clinical dementia: 6.4%	Milk: <4 servings/week to almost daily	Almost daily milk intake associated with significantly lower likelihood of vascular dementia, compared to consuming milk less than four times per week (OR = 0.35, 95% CI = 0.14–0.77)	
Eskelinen et al. [8]	Logistic regression ANCOVA	Clinical MCI: 5.7%	Fat intake from milk products and spreads, g	High SFA intakes from milk products and spreads (>21.6 g) associated with increased risk for MCI compared to those with intakes less than this (OR = 2.36, 95% CI = 1.17–4.74) High SFA from milk products associated with poorer global cognitive function (MMSE) ($p < 0.05$) High total fat from milk products and spreads associated with poorer psychomotor speed ($p < 0.05$)	Stratified by gender: primarily significant in women
Vercambre et al. [14]	Logistic regression	Cognitive decline: 12.4%	Mean intakes in g/day; no consumption compared with consumption \leq median, and $>$ median intake	Consumption of dairy desserts and ice cream associated with cognitive decline (OR = 1.33, 95% CI = 1.07–1.65)	No significant associations between milk and yogurt, and cheese consumption with cognitive decline

ANOVA = Analysis of variance; ANCOVA = analysis of covariance; BMI = body mass index; CHD = coronary heart disease; CI = confidence interval; FUD = follow-up duration; MMSE = Mini-Mental State Examination; OR = odds ratio; PUFA = polyunsaturated fatty acids; SFA = saturated fatty acids.

dairy consumption in terms of cognitive function or MCI/dementia risk. Cross-sectionally, low intakes of milk or dairy products were associated with poorer cognitive function in elderly women [11], but no significant differences for men were found. High cheese intake was associated with lower odds of cognitive impairment in the elderly [12], but no association between milk intake and cognitive impairment was found in 2 studies [10, 12]. One prospective study indicated that milk intake was associated with a significantly lower likelihood of vascular dementia in older age amongst both men and women [15].

Three studies found adverse effects on cognitive or psychological health from dairy fat. The CAIDE studies did not examine dairy intake per se, but evaluated associations of the fat from milk products and spreads with risk of MCI, dementia, AD, and a number of cognitive domains [8, 9]. High-saturated or total fat intakes were associated with an increased risk for MCI, poorer global cognitive function and poorer psychomotor speed [8], but not with risk of dementia or AD [9]. Similarly, an Australian study of elderly men demonstrated that whole-fat milk consumption was associated with impaired cognitive function [13], while the final study reported that higher consumption of dairy desserts and ice cream was associated with an increased risk for cognitive decline amongst elderly French women [14]. No significant associations were found between milk and yogurt, or cheese consumption and cognitive decline [14].

Two studies also examined relationships between dairy intake and depression [10, 13]. A higher prevalence of depressive symptoms was found in men and women with lower milk intakes [10], and whole-fat milk consumption was associated with poor mental health in elderly men [13].

Discussion

This systematic review identified 8 observational studies that examined the relationship between dairy consumption and cognitive performance. None of the observational studies identified had dairy intake as their primary focus, but instead examined dairy as a component of dietary intake. The limited available literature supports the concept that high dairy consumption may be associated with a lower likelihood of cognitive impairment, however high intakes of full-fat dairy and/or dairy fats may be associated with declines in cognitive performance. The best evidence for elucidating the effects of dairy intake on cognition will come from randomised,

clinical intervention studies but there is no evidence available from such studies at present.

Methodological Considerations/Limitations

There are many limitations to the current research and unanswered questions remain. Given that all of the studies were cross-sectional or prospective in design it is not possible to determine cause and effect of dairy consumption on cognitive measures. The evidence to suggest that a higher consumption of dairy foods may be associated with better cognition is based on a small number of cross-sectional research papers, and 1 prospective study. Therefore, definitive conclusions regarding cause and effect between dairy intake and cognition cannot be made.

Most studies (7 out of 8) attempted to control for potential confounding variables, yet 3 of these only adjusted for socio-demographic status. Incomplete adjustment for possible confounding factors might falsely indicate an association. It cannot be ruled out that people who have high dairy intakes might also have other lifestyle characteristics, for example regular exercise habits, which have not been controlled for, and which might account for the relationship with cognitive health. As with any health research, it is often the more 'healthy', or those that are more health conscious, that are interested in volunteering to participate. Similarly, the presence of illness such as vascular disease may influence any relationship between diet and cognition, and needs to be taken into account in any nutritional epidemiology research. Those with poor cognitive function or dementia may have poorer dietary patterns or awareness, which could result in lower dairy intakes. Therefore, the possibility of reverse causation also cannot be ruled out. It remains unknown as to how deteriorating cognition may impact upon food selection or dietary behaviour. The quality of food intake by participants of varying cognitive abilities was not addressed in any of the included studies. The 3 studies that had the most adequate adjustment for confounders had 3 of the highest methodological appraisal scores, were all longitudinal studies and interestingly, were the studies that found associations between dairy fat consumption and cognitive decline [8, 9, 14].

Despite the wide-ranging use of cognitive measures in the reviewed papers, they were well described, and all provided clear definitions of what constituted 'cognitive impairment or decline', described by either a cut-off score or clinical diagnosis. However, the widespread use in all studies of non-specific global screening tools to measure cognition limits the scope of information available. Many of these screening tools have demographic biases in score

distributions, have not been suitably validated in community samples representative of the populations evaluated, and do not assess different cognitive domains [16]. These tools also do not typically provide a wide range of scores to assess variability in cognitively healthy populations and are not sensitive to subtle cognitive effects that may occur. Only 1 study reviewed [8] used a battery of standardised psychological tests to assess cognitive function. Thus, while overall relationships between dairy intake and cognitive health were determined, the ability to discriminate between effects on different cognitive domains to determine their clinical relevance is very limited because of the assessment instruments used.

The description of dairy intake, including specific dairy products, average intakes, serving sizes, and fat content were poorly reported in the included studies. Three of the 6 studies which used food frequency questionnaires as the primary dietary measure did not provide a reference for the questionnaire used or report on either reliability or validity [9, 13, 15]. Only 2 papers made reference to the validity of the dietary measure used [8, 14]. Two studies assessed milk only [13, 15], 1 study assessed milk and cheese [12], and 1 study assessed 5 individual dairy foods (milk, cheese, yogurt, dairy desserts and ice cream) [14]. The 2 CAIDE studies [8, 9] also examined intake of milk products, but had more specific aims of examining relationships between dietary fat intake (from milk products and spreads) and cognitive impairment. The papers provided measures of fat intakes (in grams) but total milk intakes were not specified. The studies by Lee et al. [11] and Avila-Funes et al. [10] did not specify the particular foods included within 'dairy products' and 'milk products', respectively. Frequency measures of milk intake in the different studies varied from 'less than once a week' [12] to 'regularly' [13] or 'daily' [15]. However, the actual quantity of milk (or dairy/milk product) consumed on these occasions, as a measure in grams or millilitres, was not specified.

No studies specified the amount, in grams or in a defined serving size (of total dairy or individual dairy products), that was associated with either a detrimental or beneficial cognitive outcome. This lack of information makes it difficult to draw conclusions regarding the optimal intake of dairy that may be associated with greater cognitive health, to directly compare outcomes of studies, or to determine whether the fat content of dairy is important in mediating any relationship between diet and cognition. Only 1 study specified the fat content of dairy [13]. Despite the CAIDE studies assessing the fat content of milk products in relation to cognition, the actual fat content was not stipulated [8, 9]. The remaining

2 prospective studies [14, 15] both measured dietary intake at baseline and had extensive follow-up times (13–30 years), and so it is most likely that the dairy consumed was whole fat, as the dietary measures were undertaken before the widespread increase in the availability of reduced fat dairy products. The measurement of diet at baseline only, as done in all included prospective studies, may not accurately reflect long-term consumption patterns, as dietary habits may not remain stable.

Possible Mechanisms of Dairy-Cognition Relationship

The vascular hypothesis of dementia, implicating neurovascular dysfunction as a fundamental part of dementia, has recently emerged from epidemiological, clinical and pathological studies [17]. Vascular pathological changes associated with ageing and cognitive impairment are also common to a number of vascular diseases. Vascular alterations such as white matter lesions have been associated with lower performance in frontal lobe tasks, including attention, memory, executive function, cognitive flexibility, sensorimotor ability, and processing speed [18–24]. This is supported by a recent systematic review which concluded that type 2 diabetes, hypertension, dyslipidemia and obesity are associated with declines in cognitive performance, namely processing speed, mental flexibility, and memory, in non-demented populations [25].

Dairy may reduce the risk for cognitive impairment by modifying vascular factors linked to these detrimental brain changes, particularly via weight reduction. Epidemiological studies, animal studies and a small number of randomised trials provide evidence for an anti-obesity effect of calcium and dairy foods [26–29]. In addition to calcium, bioactive compounds derived from whey protein in dairy may contribute to accelerating weight and fat loss [26, 28–30].

Other components of dairy may play a role in reducing metabolic risk. Dairy products are the primary dietary source of vitamin D [31], which through its role in regulating calcium homeostasis may improve insulin sensitivity and glucose homeostasis [31, 32]. Phosphorus and magnesium are involved in blood pressure regulation [33, 34]. Magnesium may also modulate vascular function through its antioxidant and anti-inflammatory properties [35]. There is also evidence to suggest that increasing dietary intake of magnesium may also help reduce cholesterol and triglycerides [36], and improve diabetes control, due to its role in glucose homeostasis [37, 38]. These components of dairy may help to prevent or decrease the vascular alterations and structural brain changes that occur with cognitive decline.

The beneficial effects of these components of dairy on vascular disease may also be mediated by an improvement in inflammatory state. Individuals with greater adiposity have an increased inflammatory state in comparison with their leaner counterparts [39, 40] which has been linked with adverse cognitive function [41–43]. Any decrease in inflammation (via weight loss, improved regulation of glucose and blood pressure) may subsequently reduce the risk for cognitive decline.

Conclusions

Despite considerable methodological variability and incomplete adjustment for covariates in some studies, findings from 2 cross-sectional and 1 prospective study suggest that dairy consumption may have a beneficial effect on cognitive function. The role of dairy-derived nutrients in the regulation of vascular pathological changes associated with ageing and cognitive impairment may underlie these associations. Conversely, findings from 4 prospective studies suggest that the consumption of whole-fat dairy products may be associated with cognitive decline in the elderly, implicating saturated fat, in particular, in this relation-

ship. A number of study limitations including the measures of both cognition and dairy intake reduce the ability to draw conclusions from this collection of research.

There have been no studies to date examining the relationship between dairy intake and cognitive function in a healthy adult population across all ages. The quality of evidence from future observational studies would be improved if detailed assessments of both diet and cognition at multiple time periods (well before the onset of cognitive decline) were included. Regular assessment and recording of dairy intake is needed, distinguishing high- from low-fat dairy, and reporting dairy intake in grams per day. Future studies should include a very thorough assessment of cognition, including tests on a range of cognitive domains. It is imperative that any future research control for all potential confounding variables, including not only socio-demographics, but lifestyle factors and vascular health. Prospective studies of sufficient duration, with detailed assessment of both diet and cognition over time, would greatly enhance understanding of the possible association between dairy and cognitive functioning. More conclusive evidence is needed from well-controlled, long-term intervention trials to confirm whether dairy intake can improve cognitive functioning.

Appendix. Methodological appraisal scores for the included studies

Author	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	T
<i>Cross-sectional</i>																					
Lee et al. [11]	0	1	1/2	1	0	1/2	1	0	1/2	0	0	1	0	1	1	0	1	0	0	0	8.0
Avila-Funes et al. [10]	1	1	0	1	1/2	0	1	0	0	0	0	1	0	1	1	0	1	0	0	1	9.5
Rahman et al. [12]	1	1	0	1	1/2	0	1/2	0	0	1/2	0	1	0	1	1	1	1	1	0	1	11.5
<i>Prospective</i>																					
Almeida et al. [13]	1	1	0	0	1	0	1/2	0	0	1	0	1	0	1	1	0	1	1	0	1	10.5
Laitinen et al. [9]	1	1	1/2	0	1/2	0	1/2	0	0	1	0	1	0	1	1	1	1	1	0	1	11.5
Yamada et al. [15]	0	1/2	0	1	1	1	1/2	0	0	1/2	0	1	1	1	1	1	1	1	0	0	11.5
Eskelinen et al. [8]	1/2	1/2	1/2	0	1/2	0	1	1/2	0	1	0	1	1	1	1	1	1	1	0	1	12.5
Vercambre et al. [14]	1	1	1	1	1	1	1/2	1	1	1/2	0	1	0	1	1	1	1	1	0	1	16.0

1 = Yes; 0 = no; 1/2 = partly; T = total.

References

1 United Nations: World Population Ageing 1950–2050. New York, United Nations, 2001.
2 Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E: Mild cognitive impairment: clinical characterization and outcome. Arch Neurol 1999;56:303–308.
3 Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, Hall K, Hasegawa K, Hendrie H, Huang Y, Jorm A, Mathers C, Menezes PR, Rimmer E, Scazufca M: Global prevalence of dementia: a Delphi consensus study. Lancet 2005;366:2112–2117.
4 Bryan J: Mechanisms and evidence for the role of nutrition in cognitive ageing. Ageing Int 2004;29:28–45.
5 Solfrizzi V, Panza F, Capurso A: The role of diet in cognitive decline. J Neural Transm 2003;110:95–110.

- 6 Tooth L, Ware R, Bain C, Purdie DM, Dobson A: Quality of reporting of observational longitudinal research. *Am J Epidemiol* 2005; 161:280–288.
- 7 Hayden JA, Cote P, Bombardier C: Evaluation of the quality of prognosis studies in systematic reviews. *Ann Intern Med* 2006;144: 427–437.
- 8 Eskelinen MH, Ngandu T, Helkala EL, Tuomilehto J, Nissinen A, Soininen H, Kivipelto M: Fat intake at midlife and cognitive impairment later in life: a population-based CAIDE study. *Int J Geriatr Psychiatry* 2008; 23:741–747.
- 9 Laitinen MH, Ngandu T, Rovio S, Helkala EL, Uusitalo U, Viitanen M, Nissinen A, Tuomilehto J, Soininen H, Kivipelto M: Fat intake at midlife and risk of dementia and Alzheimer's disease: a population-based study. *Dement Geriatr Cogn Disord* 2006;22: 99–107.
- 10 Avila-Funes JA, Garant MP, Aguilar-Navarro S: Relationship between determining factors for depressive symptoms and for dietary habits in older adults in Mexico. *Rev Panam Salud Publica* 2006;19:321–330.
- 11 Lee L, Kang SA, Lee HO, Lee BH, Park JS, Kim JH, Jung IK, Park YJ, Lee JE: Relationships between dietary intake and cognitive function level in Korean elderly people. *Public Health* 2001;115:133–138.
- 12 Rahman A, Sawyer Baker P, Allman RM, Zamrini E: Dietary factors and cognitive impairment in community-dwelling elderly. *J Nutr Health Aging* 2007;11:49–54.
- 13 Almeida OP, Norman P, Hankey G, Jamrozik K, Flicker L: Successful mental health aging: results from a longitudinal study of older Australian men. *Am J Geriatr Psychiatry* 2006;14:27–35.
- 14 Vercambre MN, Boutron-Ruault MC, Ritchie K, Clavel-Chapelon F, Berr C: Long-term association of food and nutrient intakes with cognitive and functional decline: a 13-year follow-up study of elderly French women. *Br J Nutr* 2009;102:419–427.
- 15 Yamada M, Kasagi F, Sasaki H, Masunari N, Mimori Y, Suzuki G: Association between dementia and midlife risk factors: the radiation effects research foundation adult health study. *J Am Geriatr Soc* 2003;51:410–414.
- 16 Cullen B, O'Neill B, Evans JJ, Coen RF, Lawlor BA: A review of screening tests for cognitive impairment. *J Neurol Neurosurg Psychiatry* 2007;78:790–799.
- 17 Dickstein DL, Walsh J, Brautigam H, Stockton SD Jr, Gandy S, Hof PR: Role of vascular risk factors and vascular dysfunction in Alzheimer's disease. *Mt Sinai J Med* 2010;77: 82–102.
- 18 Akisaki T, Sakurai T, Takata T, Umegaki H, Araki A, Mizuno S, Tanaka S, Ohashi Y, Iguchi A, Yokono K, Ito H: Cognitive dysfunction associates with white matter hyperintensities and subcortical atrophy on magnetic resonance imaging of the elderly diabetes mellitus Japanese elderly diabetes intervention trial (J-EDIT). *Diabetes Metab Res Rev* 2006;22:376–384.
- 19 Soderlund H, Nilsson LG, Berger K, Breteiler MM, Dufouil C, Fuhrer R, Giampaoli S, Hofman A, Pajak A, de Ridder M, Sans S, Schmidt R, Launer LJ: Cerebral changes on MRI and cognitive function: the cascade study. *Neurobiol Aging* 2006;27:16–23.
- 20 Verdelho A, Madureira S, Ferro JM, Basile AM, Chabriet H, Erkinjuntti T, Fazekas F, Hennerici M, O'Brien J, Pantoni L, Salvadori E, Scheltens P, Visser MC, Wahlund LO, Waldemar G, Wallin A, Inzitari D, Study L: Differential impact of cerebral white matter changes, diabetes, hypertension and stroke on cognitive performance among non-disabled elderly. The LADIS study. *J Neurol Neurosurg Psychiatry* 2007;78:1325–1330.
- 21 Wright CB, Festa JR, Paik MC, Schmiedigen A, Brown TR, Yoshita M, DeCarli C, Sacco R, Stern Y: White matter hyperintensities and subclinical infarction: associations with psychomotor speed and cognitive flexibility. *Stroke* 2008;39:800–805.
- 22 Rabbitt P, Mogapi O, Scott M, Thacker N, Lowe C, Horan M, Pendleton N, Jackson A, Lun D: Effects of global atrophy, white matter lesions, and cerebral blood flow on age-related changes in speed, memory, intelligence, vocabulary, and frontal function. *Neuropsychology* 2007;21:684–695.
- 23 Tiehuis AM, Vincken KL, van den Berg E, Hendrikse J, Manschot SM, Mali WP, Kappelle LJ, Biessels GJ: Cerebral perfusion in relation to cognitive function and type 2 diabetes. *Diabetologia* 2008;51:1321–1326.
- 24 Breteler MM, van Amerongen NM, van Swieten JC, Claus JJ, Grobbee DE, van Gijn J, Hofman A, van Harskamp F: Cognitive correlates of ventricular enlargement and cerebral white matter lesions on magnetic resonance imaging. The Rotterdam study. *Stroke* 1994;25:1109–1115.
- 25 van den Berg E, Kloppenborg RP, Kessels RP, Kappelle LJ, Biessels GJ: Type 2 diabetes mellitus, hypertension, dyslipidemia and obesity: a systematic comparison of their impact on cognition. *Biochim Biophys Acta* 2009; 1792:470–481.
- 26 Zemel MB: Role of calcium and dairy products in energy partitioning and weight management. *Am J Clin Nutr* 2004;79:907S–912S.
- 27 Zemel MB, Teegarden D, Van Loan MD, Schoeller DA, Matkovic V, Lyle RM, Craig BA: Dairy-rich diets augment fat loss on an energy-restricted diet: a multicenter trial. *Nutrients* 2009;1:83–100.
- 28 Teegarden D: The influence of dairy product consumption on body composition. *J Nutr* 2005;135:2749–2752.
- 29 Zemel MB: The role of dairy foods in weight management. *J Am Coll Nutr* 2005;24:537S–546S.
- 30 Luhovyy BL, Akhavan T, Anderson H: Whey proteins in the regulation of food intake and satiety. *J Am Coll Nutr* 2007;26:704S–712S.
- 31 Teegarden D, Donkin SS: Vitamin D: emerging new roles in insulin sensitivity. *Nutr Res Rev* 2009;22:82–92.
- 32 von Hurst PR, Stonehouse W, Coad J: Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient – a randomised, placebo-controlled trial. *Br J Nutr* 2010;103:549–555.
- 33 Alonso A, Nettleton JA, Ix JH, de Boer IH, Folsom AR, Bidulescu A, Kestenbaum BR, Chambless LE, Jacobs DR Jr: Dietary phosphorus, blood pressure, and incidence of hypertension in the atherosclerosis risk in communities study and the multi-ethnic study of atherosclerosis. *Hypertension* 2010;55:776–784.
- 34 Sontia B, Touyz RM: Role of magnesium in hypertension. *Arch Biochem Biophys* 2007; 458:33–39.
- 35 Weglicki WB, Mak IT, Kramer JH, Dickens BF, Cassidy MM, Stafford RE, Philips TM: Role of free radicals and substance p in magnesium deficiency. *Cardiovasc Res* 1996;31: 677–682.
- 36 Singh RB, Rastogi SS, Sharma VK, Saharia RB, Kulshretha SK: Can dietary magnesium modulate lipoprotein metabolism? *Magn Trace Elem* 1990;9:255–264.
- 37 Ma B, Lawson AB, Liese AD, Bell RA, Mayer-Davis EJ: Dairy, magnesium, and calcium intake in relation to insulin sensitivity: approaches to modeling a dose-dependent association. *Am J Epidemiol* 2006;164:449–458.
- 38 Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A: Magnesium. An update on physiological, clinical and analytical aspects. *Clin Chim Acta* 2000;294:1–26.
- 39 Festa A, D'Agostino R, Williams K, Karter AJ, Mayer-Davis EJ, Tracy RP, Haffner SM: The relation of body fat mass and distribution to markers of chronic inflammation. *Int J Obes* 2001;25:1407–1415.
- 40 Pannaciuoli N, Cantatore FP, Minenna A, Bellacicco M, Giorgino R, De Pergola G: C-reactive protein is independently associated with total body fat, central fat, and insulin resistance in adult women. *Int J Obes* 2001; 25:1416–1420.
- 41 Schmidt R, Schmidt H, Curb JD, Masaki K, White LR, Launer LJ: Early inflammation and dementia: a 25-year follow-up of the Honolulu-Asia Aging Study. *Ann Neurol* 2002; 52:168–174.
- 42 Yaffe K, Kanaya A, Lindquist K, Simonsick EM, Harris T, Shorr RI, Tykavsky FA, Newman AB: The metabolic syndrome, inflammation, and risk of cognitive decline. *JAMA* 2004;292:2237–2242.
- 43 Yaffe K, Lindquist K, Penninx BW, Simonsick EM, Pahor M, Kritchevsky S, Launer L, Kuller L, Rubin S, Harris T: Inflammatory markers and cognition in well-functioning African-American and white elders. *Neurology* 2003;61:76–80.

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