

## **SUPPLEMENTAL MATERIAL**

### **CONTENT**

#### Supplemental methods

- Supplement I. MOOSE Checklist
- Supplement II. Search strategy
- Supplement III. Quality assessment of cohort studies on dairy intake and stroke risk.
- Supplement IV: Definition of dairy foods as described in the individual cohort studies included in the meta-analyses

## Supplement I MOOSE checklist<sup>1</sup>

	Reported on page	Comments
<b>Reporting of background should include</b>		
Problem definition	3	
Hypothesis statement	3	
Description of study outcome(s)	3	
Type of exposure or intervention used	3	
Type of study designs used	3	
Study population	3	
<b>Reporting of search strategy should include</b>		
Qualifications of searchers (e.g. librarians and investigators)	4	
Search strategy, including time period used in the synthesis and key words	4, Supplement II	
Effort to include all available studies, including contact with authors	4	
Databases and registries searched	4	
Search software used, name and version, including special features used (e.g. explosion)	4	
Use of hand searching (e.g. reference lists of obtained articles)	4	
List of citations located and those excluded, including justification	4	
Method of addressing articles published in languages other than English	4	
Method of handling abstracts and unpublished studies	4	
Description of any contact with authors	4	
<b>Reporting of methods should include</b>		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	4	
Rationale for the selection and coding of data (e.g. sound clinical principles or convenience)	4	
Documentation of how data were classified and coded (e.g. multiple raters, blinding and interrater reliability)	4	
Assessment of confounding (e.g. comparability of cases and controls in studies where appropriate)	4	
Assessment of study quality, including blinding of	5	

quality assessors, stratification or regression on possible predictors of study results		
Assessment of heterogeneity	6	
Description of statistical methods (e.g. complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	5-6	
Provision of appropriate tables and graphics	Supplementary files	
<b>Reporting of results should include</b>		
Graphic summarizing individual study estimates and overall estimate	27-53	
Table giving descriptive information for each study included	17-22	
Results of sensitivity testing (e.g. subgroup analysis)	7-9	
Indication of statistical uncertainty of findings	7-9	By CI's and I <sup>2</sup>
<b>Reporting of discussion should include</b>		
Quantitative assessment of bias (e.g. publication bias)	8, Fig 4-5	
Justification for exclusion (e.g. exclusion of non-English language citations)	Na	
Assessment of quality of included studies	10	
<b>Reporting of conclusions should include</b>		
Consideration of alternative explanations for observed results	10	
Generalization of the conclusions (i.e. appropriate for the data presented and within the domain of the literature review)	11	
Guidelines for future research	12	
Disclosure of funding source	13	

## Supplement II Search strategy (Pubmed) – updated until June 2015

EMBASE (<http://www.embase.com>) and SCOPUS (<http://www.scopus.com>) search strategies were based on the Pubmed (<http://www.ncbi.nlm.nih.gov/pubmed>) query syntax shown below.

### ACTION 1 DETERMINANTS

#1 dairy products[Mesh] OR milk[Mesh] OR cheese[Mesh] OR yogurt[Mesh] OR butter[Mesh] OR cultured milk products[Mesh] OR ice cream[Mesh]

#2 dairy[tiab] OR milk\*[tiab] OR cheese\*[tiab] OR yogurt\*[tiab] OR yoghurt\*[tiab] OR butter[tiab] OR buttermilk[tiab] OR custard\*[tiab] OR pudding\*[tiab] OR cream\*[tiab] OR cream[tiab] OR ice cream[tiab] OR ice-cream[tiab] OR curd\*[tiab] OR porridge[tiab]

#3 (#1 OR #2)

### ACTION 2 OUTCOME

#4 mortality[tiab] OR death\*[tiab] OR dead[tiab] OR all-cause[tiab] OR all cause[tiab] OR fatal[tiab] OR event[tiab] OR nonfatal[tiab] OR non-fatal[tiab] OR Mortality[Mesh:NoExp] OR mortality[Mesh subheading]

#5 cardiovascular[tiab] OR vascular[tiab] OR CVD[tiab] OR Cardiovascular Diseases[Mesh:NoExp]

#6 cerebrovascular[tiab] OR stroke[tiab] OR TIA[tiab] OR transient ischemic\*[tiab] OR CVA[tiab] OR cerebral infarction[tiab] OR Cerebrovascular accident[Mesh:NoExp] OR stroke[Mesh:NoExp]

#7 #4 OR #5 OR #6

### ACTION 3 COMBINE EXPOSURE AND OUTCOME

#8 #3 AND #7

### ACTION 4 LIMITS

#9 ((animals[MeSH] NOT (humans[MeSH] AND animals[MeSH])))

#10 #8 NOT #9

#11 breast [tiab]

#12 #10 NOT #11

1 Supplement III. Quality assessment of cohort studies on dairy intake and risk of stroke

	Selection				Comparability	Outcome			Total score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study		Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Follow up long enough for outcomes to occur	
Bernstein et al., 2012 - HPFS <sup>2</sup>	C	A★	C	A★	A★B★	B★	A★	B★	7
Bernstein et al., 2012 - NHS <sup>2</sup>	C	A★	C	A★	A★B★	B★	A★	B★	7
Dalmeijer et al., 2013 <sup>3</sup>	A★	A★	B★	A★	A★B★	B★	A★	B★	9
Elwood et al., 2004 <sup>4</sup>	A★	A★	C	A★	A★	B★	A★	B★	7
Goldbohm et al., 2011 <sup>5</sup>	A★	A★	B★	A★	A★B★	B★	A★	B★	9
Iso et al., 1999 <sup>6</sup>	C	A★	B★	A★	A★	B★	A★	B★	7
Kinjo et al., 1999 <sup>7</sup>	A★	A★	C	A★	.	B★	A★	D	5
Kondo et al., 2013 <sup>8</sup>	A★	A★	B★	A★	A★	B★	A★	B★	8

	Selection				Comparability	Outcome			
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Follow up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total score
Larsson et al., 2009 <sup>9</sup>	C	A★	B★	A★	A★B★	B★	A★	D	7
Larsson et al., 2012 <sup>10</sup>	A★	A★	B★	A★	A★B★	B★	A★	B★	9
Lin 2013 et al., 2013 <sup>11</sup>	A★	A★	C	A★	.	A★	A★	A★	6
Louie al., 2013 <sup>12</sup>	B★	A★	B★	A★	A★	B★	A★	A★	8
Misirli et al., 2012 <sup>13</sup>	A★	A★	C	A★	A★	B★	A★	D	6
Ness et al., 2001 <sup>14</sup>	C	A★	D	A★	.	C	A★	D	3
Pan et al., unpublished	C	A★	C	A★	A★B★	B★	A★	B★	7
Praagman et al., 2015 <sup>15</sup>	A★	A★	B★	A★	A★B★	A★	A★	D	8
Sauvaget et al., 2003 <sup>16</sup>	A★	A★	C	A★	.	B★	A★	B★	6

	Selection				Comparability	Outcome			
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Follow up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total score
Sonestedt et al., 2011 <sup>17</sup>	B★	A★	A★	A★	A★B★	A★	A★	A★	9
Yaemsiri et al., 2012 <sup>18</sup>	B★	A★	C	A★	A★B★	B★	A★	C	7

## NEWCASTLE – OTTAWA QUALITY ASSESSMENT SCALE COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

### **Selection**

#### 1) Representativeness of the exposed cohort

- a) truly representative of the average *healthy adults* in the community ★
- b) somewhat representative of the average *healthy adults* in the community ★
- c) selected group of users *e.g. nurses, volunteers, smokers*
- d) no description of the derivation of the cohort

#### 2) Selection of the non-exposed cohort

- a) drawn from the same community as the exposed cohort ★
- b) drawn from a different source
- c) no description of the derivation of the non-exposed cohort

#### 3) Ascertainment of exposure

- a) secure record (*e.g. 7 day food diary*) ★
- b) structured interview/ $\geq 2$  *dietary recalls/diet history/ food frequency questionnaire validated for dairy or calcium* ★
- c) written self-report (*e.g. <2 dietary recalls/non-validated food frequency questionnaire or not reported whether food frequency questionnaire was validated for dairy*)
- d) no description

#### 4) Demonstration that outcome of interest was not present at start of study

- a) yes ★
- b) no

### **Comparability**

#### 1) Comparability of cohorts on the basis of the design or analysis

- a) study controls for *age, sex, body mass index, smoking, and total energy intake* ★
- b) study controls for any additional factor (*e.g. physical activity, dietary factors*) ★

### **Outcome**

#### 1) Assessment of outcome

- a) independent blind assessment/*Complete medical information available* ★
- b) record linkage/*Medical records or validated self-report* ★
- c) non-validated self-report
- d) no description

#### 2) Was follow-up long enough for outcomes to occur



a) yes ★

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ★

b) subjects lost to follow up unlikely to introduce bias - small number lost  $\leq 20\%$  follow up, or description provided of those lost ★

c) follow up rate  $< 80\%$  or no description of those lost

d) no statement

## Supplement IV

### Definition of dairy products as described in the papers of 18 prospective cohort studies included in the meta-analyses (in alphabetical order)

Exposure category original paper	Exposure category meta-analysis	Detailed description if available
<i>Bernstein 2011</i> <sup>2</sup>		
Whole fat dairy	High-fat dairy	whole milk, ice cream, hard cheese, full fat cheese, cream, sour cream, cream cheese, butter
Low-fat dairy	Low-fat dairy	skim/low-fat milk, 1% and 2% milk, yogurt, cottage and ricotta cheeses, low-fat cheese, sherbet
<i>Dalmeijer 2013</i> <sup>3</sup>		
Total dairy	Total dairy	All dairy food products, except butter and ice-cream
Milk and milk products	Milk	All kinds of milk, yogurt, coffee creamers, curd, pudding, porridge, custard, and whipping cream
Fermented dairy	Fermented dairy	Buttermilk, yogurt, cheese
Cheese	Cheese	All types of cheese, except for curd
High-fat dairy	High-fat dairy	Milk and milk products with a fat content $\geq 2\text{g}/100\text{g}$ (whole milk products) or cheese products with a fat content $\geq 20\text{g}/100\text{g}$ .
Low-fat dairy	Low-fat dairy	Milk and milk products with a fat content $< 2\text{g}/100\text{g}$ (skimmed or semi-skimmed milk products), or cheese with a fat content $< 20\text{g}/100\text{g}$ .
<i>Elwood 2004</i> <sup>4</sup>		
Milk	Milk	Liquid milk, not milk used in food preparation
<i>Goldbohm 2011</i> <sup>5</sup>		
Milk products	Milk	
Non-fermented full-fat milk	High-fat milk	Whole milk (3.7% fat), cream (36%, 20% fat), condense whole milk, whole-milk cocoa, pudding, ice cream
Non-fermented low-fat milk	Low-fat milk	Low-fat milk (1.5% fat), skim milk (0.1% fat, condensed low-fat milk, low-fat and skim cocoa
Fermented full-fat milk	-	Yogurt (3.5% fat, full-fat quark (fresh cheese), sour cream
Fermented low-fat milk	Fermented dairy*	Buttermilk, skim yogurt (0.1% fat) nonfat quark (fresh cheese)
Cheese	Cheese	
Fat cheese	-	Not further defined
Low-fat cheese	-	Not further defined
Butter	Butter	
Low-fat dairy	Low-fat dairy	

<i>Iso 1999<sup>6</sup></i>		
Milk	Milk	Not further defined
Low-fat milk	Low-fat milk	Not further defined
Whole-fat milk	High-fat milk	Not further defined
Yogurt	Yogurt	Not further defined
Cheese	Cheese	Not further defined
<i>Kinjo 1999<sup>7</sup></i>		
Dairy milk	Milk	Not further defined
<i>Kondo 2013<sup>8</sup></i>		
Milk and dairy products	Milk	Authors reported that 93% comprises milk
<i>Larsson 2009<sup>9</sup></i>		
Total dairy	Total dairy	Low-fat milk, whole milk, yogurt, cheese, cream, ice-cream, butter (dairy from mixed dishes included)
Low-fat milk	Low-fat milk	Not further defined
Whole milk	High-fat milk	Not further defined
Total milk (additionally provided by the author)	Milk	
Sour milk	-	
Yogurt	Yogurt	
Cheese	Cheese	
Cream	-	
Ice cream	-	
Butter	Butter	
<i>Larsson 2012<sup>10</sup></i>		
Total dairy	Total dairy	Low-fat milk (0.5% fat), medium-fat milk (1.5%), full-fat milk (3% fat), milk in pancakes, low-fat sour milk/yogurt (0.5% fat), full-fat sour milk/yogurt (3% fat), cottage cheese (4% fat), low-fat cheese (10-17% fat), full-fat cheese (~28% fat), ice cream, cream, crème fraîche
Low-fat dairy	Low-fat dairy	Low-fat milk, medium-fat milk, low-fat sour milk/yogurt, medium-fat sour milk/yogurt, cottage cheese, low-fat cheese
Full-fat dairy	High-fat dairy	Full-fat milk, full-fat sour milk/yogurt, full-fat cheese, ice cream, cream, crème fraîche
Milk	Milk	Low-fat milk, medium-fat milk, full-fat milk, milk in pancakes
Sour milk and yogurt	Fermented dairy*	
Cheese	Cheese	Low-fat cheese, full-fat cheese
Cream and crème fraîche	-	
<i>Lin 2013<sup>11</sup></i>		
Dairy	Milk	According to the authors, almost all dairy comprised milk

<i>Louie 2013<sup>12</sup></i>		
Total dairy	Total dairy	All dairy foods
Low-fat dairy	Low-fat dairy	Reduced fat/skim milk, reduced fat dairy dessert, low-fat cheese
Whole-fat dairy	High-fat dairy	Whole fat milk, whole fat cheese, medium fat dairy dessert
Ratio Low-fat dairy: whole fat dairy	-	
<i>Misirli 2012<sup>13</sup></i>		
Dairy products	Total dairy	Not further defined
<i>Ness 2001<sup>14</sup></i>		
Milk	Milk	Not further defined
<i>Pan (unpublished results)</i>		
Total dairy	Total dairy	Not further defined
Milk	Milk	Not further defined
<i>Praagman 2015<sup>15</sup></i>		
Dairy products	Total dairy	Milk, buttermilk, yogurt, coffee creamer, curd, pudding, porridge, custard, whipped cream, ice cream, cheese (not butter)
Low-fat dairy	Low-fat dairy	Milk and milk products with a fat content of <2g/100g and cheese products with a fat content of <20g/100g
High-fat dairy	High-fat dairy	Milk and milk products with a fat content of ≥2g/100g and cheese products with a fat content of ≥20g/100g
Total milk	Milk	All types of dairy, excluding cheese
Fermented dairy	Fermented dairy	All types of buttermilk, yogurt, curd, and cheese
Cheese	Cheese	All types of cheese, excluding curd
Yogurt	Yogurt	
<i>Sauvagat 2003<sup>16</sup></i>		
Dairy products	-	Butter, cheese
Milk	Milk	Milk
<i>Sonestedt 2011<sup>17</sup></i>		
Total dairy	Total dairy	Milk, cheese (>10% fat), cream, butter, milk-based spread Bregott
Milk	Milk	Non-fermented milk, fermented milk
Non-fermented milk	-	
Fermented milk	Fermented dairy*	Yogurt, processed sour milk
Low-fat milk	Low-fat milk	≤2.4% fat
High-fat milk	High-fat milk	>2.4% fat
Cheese	Cheese	>10% fat
Butter	Butter	Butter, milk-based spread Bregott
Cream	-	
<i>Yaemsiri 2012<sup>18</sup></i>		
Total dairy	Total dairy	Not further defined

\* Fermented milk includes cheese, yogurt and sour milk. We included studies that combined at least two of these products in our analysis of fermented dairy.

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2. Bernstein AM, Pan A, Rexrode KM, Stampfer M, Hu FB, Mozaffarian D, Willett WC. Dietary protein sources and the risk of stroke in men and women. *Stroke*. 2012;43:637-644.
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