**Supplementary Table 2.**

**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 communityC:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) somewhat representative of the average *healthy adults* in the community C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

c) selected group of users *e.g. nurses, volunteers, vegetarian*

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 cohortC:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

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)* C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) structured interview/≥ 2 *dietary recalls/diet history/ food frequency questionnaire validated for dairy components* C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

c) written self-report (*e.g. <2 dietary recalls/non-validated food frequency questionnaire or not reported whether food frequency questionnaire was validated*)

d) no description

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

a) yesC:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) no

**Comparability**

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

a) study controls for *age, sex, smoking, total energy intake, and body mass index*C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) study controls for any additional factor (*e.g. physical activity, alcohol intake, family history of diabetes, dietary factors*) C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

**Outcome**

1) Assessment of outcome

a) independent blind assessment (e.g. clinical diagnosis/complete medical information available).C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) record linkage/*medical record or validated self-report* C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

c) non-validated self-report

d) no description   
2) Was follow-up long enough for outcomes to occur

a) yes/ *follow up period for outcome of interest is 10 years or over* C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) no

3) Adequacy of follow-up of cohorts

a) complete follow-up - all subjects accounted for C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

b) subjects lost to follow-up unlikely to introduce bias - small number lost ≤*20%* follow-up, or description provided of those lost C:\Users\gijsb008\AppData\Local\Microsoft\Windows\Temporary Internet Files\Content.IE5\J2VJHQRN\star-silhouette[1].jpg

c) follow-up rate <*80%* or no description of those lost

d) no statement

|  |  |  |
| --- | --- | --- |
| **Supplementary Table 1. Search terms and strategy for papers indexed in PUBMED** | | |
| **No** | **Concept** | **Search terms** |
| **1** | **Choline** | “Choline” [Text Word] OR “phosphatidylcholine” [Text Word] OR “phosphatidyl-choline” [Text Word] |
| **2** | **Mortality** | 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] |
| **3** | **Cardiovascular** | cardiovascular[tiab] OR vascular[tiab] OR CVD[tiab] OR Cardiovascular Diseases[Mesh:NoExp] |
| **4** | **Stroke** | 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] |
| **5** | **Combination** | #1 OR #2 OR #3 OR #4 |
| **6** | **Combination Exposure And Outcome** | #1 AND #5 |
| **7** | **Limit** | Rats[Mesh:NoExp]) OR Mice[Mesh:NoExp]) OR rat[Title/Abstract]) OR rats[Title/Abstract]) OR mouse[Title/Abstract]) OR mice[Title/Abstract]) OR vivo[Title/Abstract]) OR vitro[Title/Abstract]) |
| **8** | **Limit** | #6 NOT #7 |

**Supplementary Table 2.** Quality assessment of cohorts studies which included in meta-analysis.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Studies** | **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** | **Adequacy of follow-up of cohorts** |
| Nagata et al, 2015(1) | C | A | B | A | A B | B | B | B | 9 |
| Zheng et al, 2016(2) | C | A | B | A | A B | B | B | B | 9 |

1. Nagata C, Wada K, Tamura T, Konishi K, Kawachi T, Tsuji M, et al. Choline and Betaine Intakes Are Not Associated with Cardiovascular Disease Mortality Risk in Japanese Men and Women. The Journal of nutrition. 2015;145(8):1787-92.

2. Zheng Y, Li Y, Rimm EB, Hu FB, Albert CM, Rexrode KM, et al. Dietary phosphatidylcholine and risk of all-cause and cardiovascular-specific mortality among US women and men. The American journal of clinical nutrition. 2016;104(1):173-80.