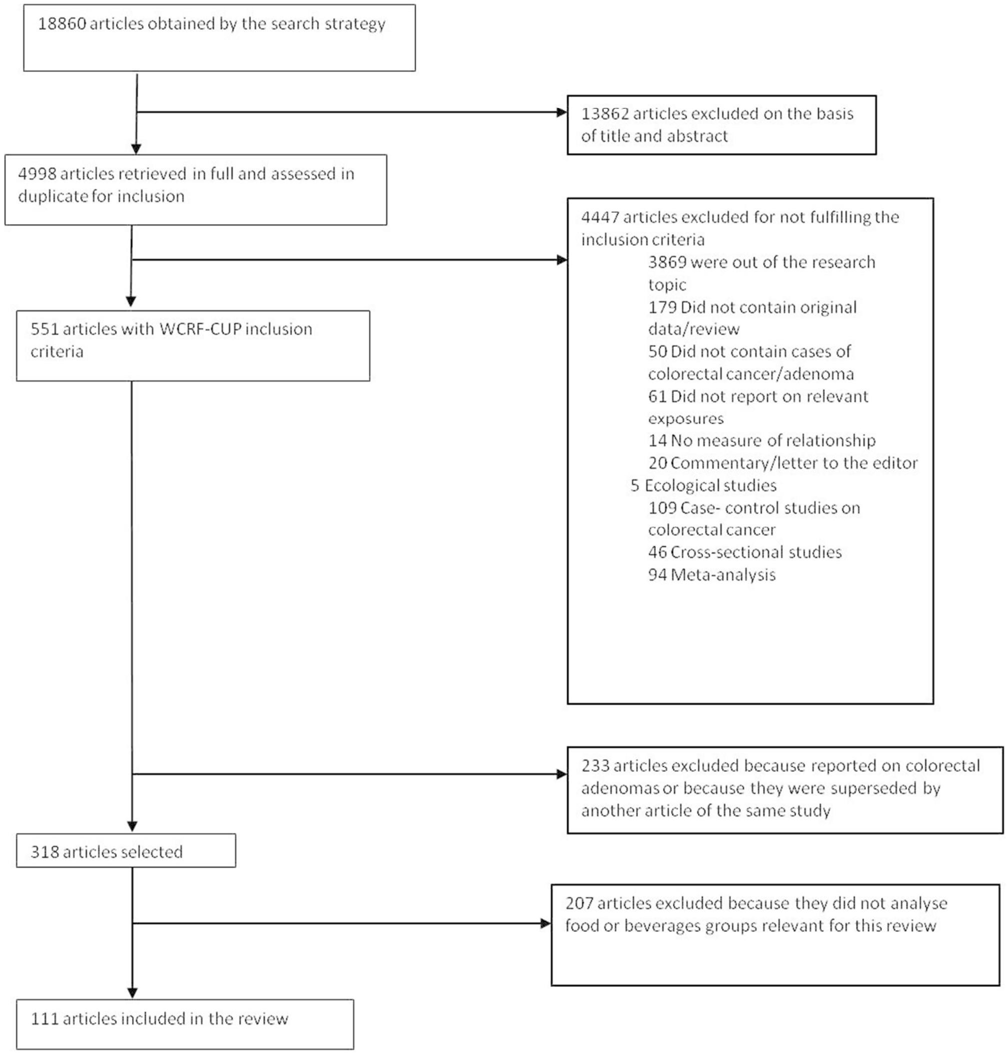


Figure 1 Flowchart of study selection. Search period January 1st 2010-May 31st 2015
Figure 1
189x198mm (150 x 150 DPI)

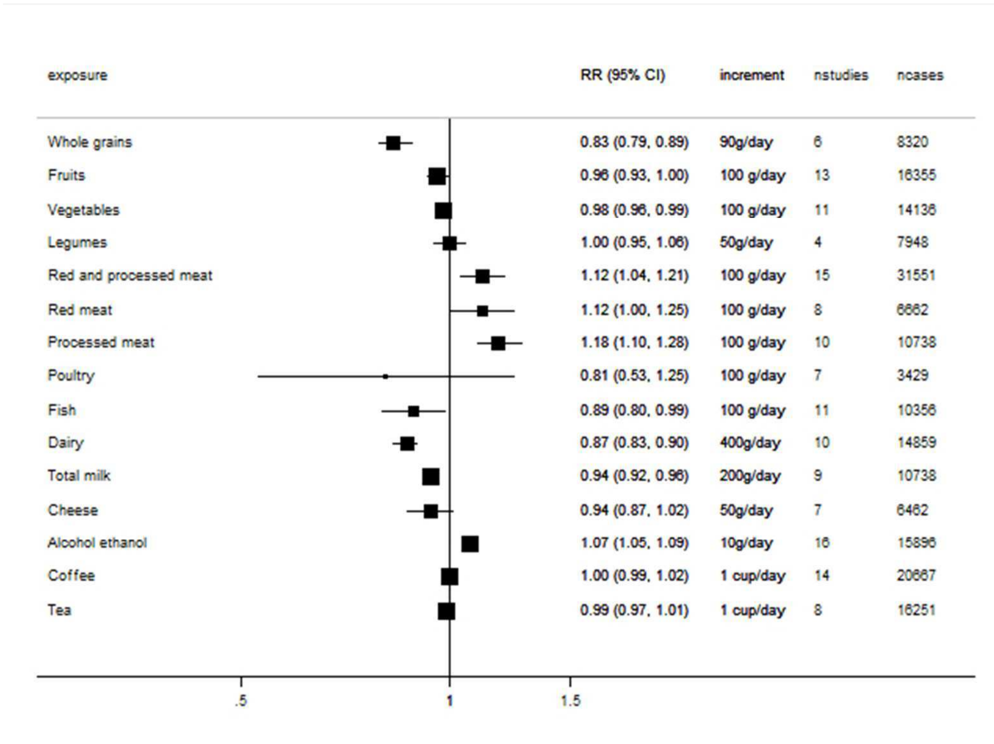


Figure 2A Dose-response meta-analysis of foods and beverages and risk of colorectal cancer
Figure 2A
225x168mm (72 x 72 DPI)

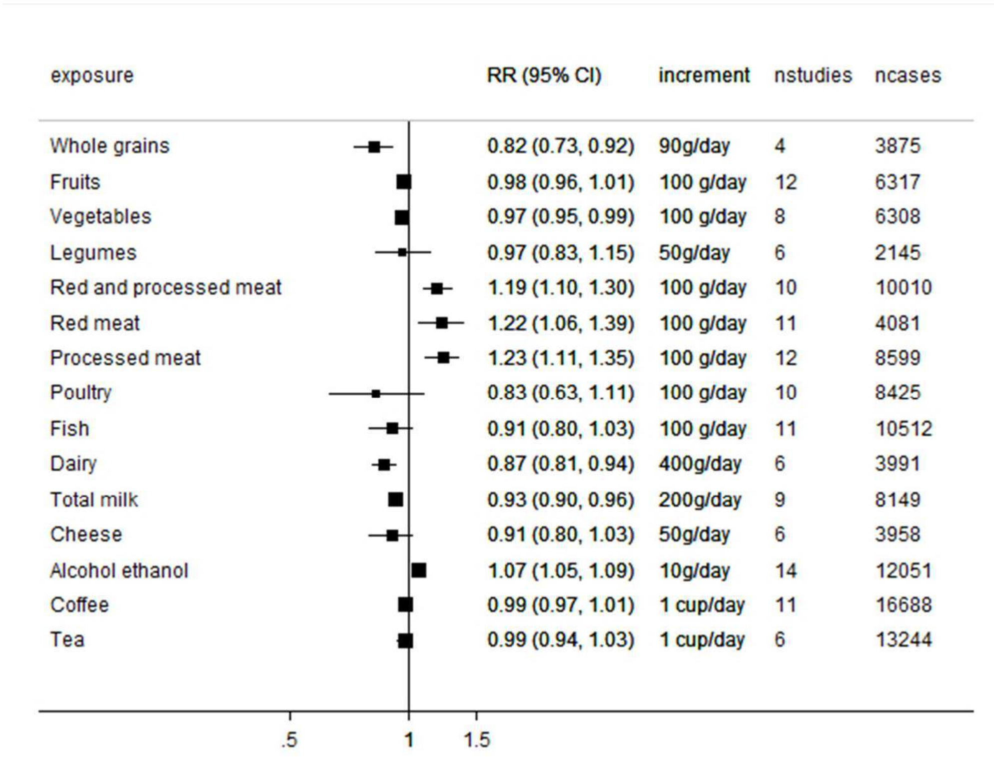


Figure 2B Dose-response meta-analysis of foods and beverages and risk of colon cancer
Figure 2B
214x168mm (72 x 72 DPI)

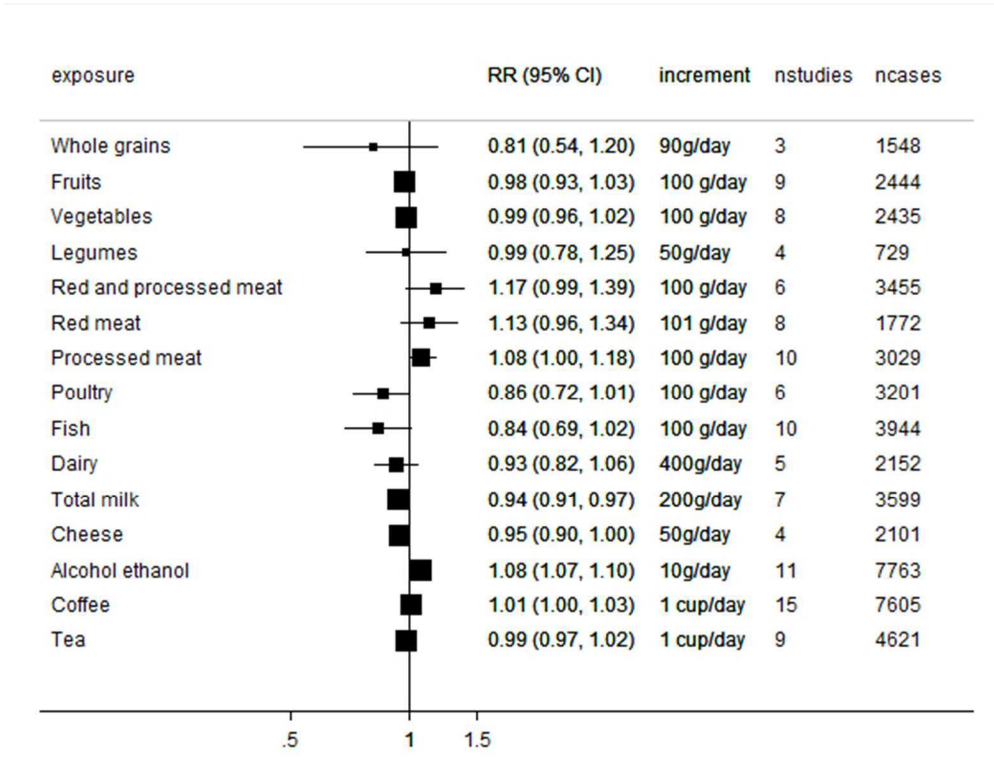


Figure 2C Dose-response meta-analysis of foods and beverages and risk of rectal cancer
Figure 2C
214x168mm (72 x 72 DPI)

**Table 1 (A –D)** Summary of results of dose-response meta-analysis for foods and beverages investigated in the 2015 CUP update by year of update (2005, 2010, 2015)

**1A** Results of dose-response meta-analysis for wholegrain, fruits and vegetables

| | 2005 SLR* | | | 2011 CUP SLR | | | 2015 CUP SLR | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Wholegrain** | | | | | | | | | |
| Increment unit | - | | | 90 g/day | | | 90 g/day | | |
| Studies (*n*) | | | | 6 | 4 | 3 | 6 | 4 | 3 |
| Cases (total number) | | | | 7941 | 3656 | 1393 | 8320 | 3875 | 1548 |
| Random effect RR (95%CI) | | | | 0.83 (0.79-0.89) | 0.86 (0.79-0.94) | 0.80 (0.56-1.14) | 0.83 (0.79-0.89) | 0.82 (0.73-0.92) | 0.81 (0.54-1.20) |
| Heterogeneity ($I^2$,*p-value* ) | | | | 18%, *p*=0.30 | 0%, *p*=0.42 | 91%, p<0.0001 | 18.2%, *p*=0.30 | 0%, *p*=0.49 | 91.2%, p<0.0001 |
| Egger's *p* value | | | | - | - | - | 0.72 | - | - |

* No data available

| | 2005 SLR | | | 2011 CUP SLR | | | 2015 CUP SLR | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Fruits and vegetables** | | | | | | | | | |
| Increment unit used | Per 1 serving/day | | | 100 g/day | | | 100 g/day | | |
| Studies (*n*) | 7 | 8 | 4 | 7 | 10 | 9 | 10 | 12 | 10 |
| Cases (total number) | - | - | - | 9932 | 5827 | 2575 | 10999 | 6045 | 2746 |
| Random effect RR (95%CI) | 0.99 (0.96-1.03) | 0.99 (0.97-1.02) | 0.98 (0.92-1.05) | 0.99 (0.97-1.00) | 0.99 (0.97-1.01) | 0.99 (0.96-1.01) | 0.98 (0.97-0.99) | 0.99 (0.97-1.00) | 0.99 (0.97-1.01) |
| Heterogeneity ($I^2$, *p-value*) | 54.6%, *p*=0.03 | 45.2%, *p*=0.09 | 51.7%, *p*=0.10 | 34.6%, *p*=0.16 | 25.4%, *p*=0.21 | 5.6%, *p*=0.39 | 13.8%, *p*=0.32 | 0%, *p*=0.50 | 0%, *p*=0.56 |
| Egger's *p* value | - | - | - | 0.76 | 0.30 | 0.78 | 0.64 | 0.75 | 0.22 |
| **Vegetables**[1] | | | | | | | | | |
| Increment unit used | Per 2 servings/day | | | 100 g/day | | | 100 g/day | | |
| Studies (*n*) | 7 | 6 | 4 | 8 | 10 | 7 | 11 | 12 | 8 |
| Cases (total number) | - | - | - | 12275 | 5772 | 2285 | 14136 | 6308 | 2435 |
| Random effect RR (95%CI) | 1.00 (0.90-1.11) | 0.96 (0.89-1.04) | 0.99 (0.81-1.21) | 0.98 (0.96-0.99) | 0.97 (0.95-1.00) | 1.00 (0.96-1.05) | 0.98 (0.96-0.99) | 0.97 (0.95-0.99) | 0.99 (0.96-1.02) |
| Heterogeneity ($I^2$, *p-value*) | 62.5% , *p*=0.006 | 8.6%, *p*=0.36 | 0%, *p*=0.51 | 0%, *p*=0.78 | 0%, *p*=0.63 | 0%, *p*=0.82 | 0%, *p*=0.48 | 0%, *p*=0.77 | 0%, *p*=0.78 |
| Egger's *p* value | - | - | - | 0.54 | 0.73 | 0.34 | 0.92 | 0.77 | 0.72 |

| | 2005 SLR* | | | 2011 CUP SLR | | | 2015 CUP SLR | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon Cancer** | **Rectal Cancer** | **Colorectal cancer** | **Colon Cancer** | **Rectal Cancer** |
| **Fruits** | | | | | | | | | |
| Increment unit used | Per 1 serving/day | | | 100 g/day | | | 100 g/day | | |
| Studies (*n*) | 8 | 7 | 3 | 8 | 10 | 7 | 13 | 12 | 9 |
| Cases (total number) | - | - | - | 12775 | 6114 | 2303 | 16355 | 6317 | 2444 |
| Random effect RR (95%CI) | 0.97 (0.92-1.03) | 0.97 (0.92-1.02) | 0.94 (0.78-1.13) | 0.97 (0.94-0.99) | 0.98 (0.95-1.01) | 0.97 (0.92-1.02) | 0.96 (0.93-1.00) | 0.98 (0.96-1.01) | 0.98 (0.93-1.03) |
| Heterogeneity ($I^2$, *p-value*) | 68.9%, *p*=0.04 | 65.3%, *p*=0.003 | 72.0%, *p*=0.03 | 51.2%, *p*=0.05 | 38.5%, *p*=0.10 | 38.4%, *p*=0.14 | 68.0%, p<0.0001 | 37.9%, *p*=0.09 | 54.9%, *p*=0.02 |
| Egger's *p* value | - | - | - | 0.60 | 0.92 | 0.70 | 0.07 | 0.55 | 0.41 |

[1] As part of the 2010 CUP SLR it was concluded that garlic probably decreases the risk of colorectal cancer. A meta-analysis including two cohort studies was conducted and showed a RR estimate of 0.66 (95% CI: 0.48-0.91, ph=0.67) for the highest category of garlic intake compared with the lowest category. A meta-analysis including five case-control studies showed a RR of 0.76 (0.58-0.98, ph=0.06). There were no new data to update the analysis on garlic.

**1B** Results of dose-response meta-analysis for dairy products, milk and cheese

| | **2005 SLR** | | | **2010 CUP SLR** | | | **2015 CUP SLR** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Dairy products[2]** | | | | | | | | | |
| Increment unit used | Per 1 serving/day | Per 200 g/d | Per 1 serving/day | 400 g/day | | | 400 g/day | | |
| Studies (*n*) | 8 | 2 | 5 | 9 | 5 | 4 | 10 | 6 | 5 |
| Cases (total number) | - | - | - | 9807 | - | - | 14859 | 3991 | 2152 |
| Random effect RR (95%CI) | 0.97 (0.93-1.01) | 0.95 (0.82-1.10) | 0.95 (0.86-1.06) | 0.85 (0.81-0.90) | 0.84 (0.72-0.97) | 1.00 (0.77-1.28) | 0.87 (0.83-0.90) | 0.87 (0.81-0.94) | 0.93 (0.82-1.06) |
| Heterogeneity ($I^2$, *p-value*) | 11.5%, *p*=0.34 | 0%, *p*=0.86 | 49.5%, *p*=0.95 | 0%, *p*=0.57 | 35.4%, *p*=0.19 | 68.9%, *p*=0.02 | 18.4%, *p*=0.27 | 24.4%, *p*=0.25 | 48.6%, *p*=0.10 |
| Egger's *p* value | - | - | - | 0.73 | - | - | 0.63 | - | - |
| **Milk** | | | | | | | | | |
| Increment unit used | Per 1 serving/day | Highest vs. lowest | Highest vs. lowest | 200 g/day | | | 200 g/day | | |
| Studies (*n*) | 6 | 6 | 2 | 9 | 9 | 7 | 9 | 9 | 7 |
| Cases (total number) | - | - | - | 4510 | - | - | 10738 | 8149 | 3599 |
| Random effect RR (95%CI) | 0.94 (0.85-1.03) | 0.79 (0.65-0.96) | 0.93 (0.59-1.46) | 0.90 (0.85-0.94) | 0.88 (0.79-0.97) | 0.90 (0.79-1.02) | 0.94 (0.92-0.96) | 0.93 (0.90-0.96) | 0.94 (0.91-0.97) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Heterogeneity ($I^2$, *p-value*) | 12.4%, *p*=0.34 | 14.9%, *p*=0.32 | 0%, *p*=0.75 | 24.6%, *p*=0.22 | 44.1%, *p*=0.11 | 0%, *p*=0.53 | 0%, *p*=0.97 | 30.0%, *p*=0.18 | 0%, *p*=0.93 |
| Egger's p value | - | - | - | 0.61 | - | - | 0.63 | 0.49 | 0.62 |

| | **2005 SLR** | | | **2010 CUP SLR*** | | | **2015 CUP SLR** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorecta l cancer** | **Colon cancer** | **Rectal cancer** |
| **Cheese** | | | | | | | | | |
| Increment unit used | Per 1 serving/day | Per 50 g/day | - | | | | 50 g/day | | |
| Studies (*n*) | 3 | 2 | - | | | | 7 | 6 | 4 |
| Cases (total number) | 583 | 484 | - | | | | 6462 | 3958 | 2101 |
| RR (95%CI) | 1.14 (0.82-1.58) | 1.11 (0.88-1.39) | - | | - | | 0.94 (0.87-1.02) | 0.91 (0.80-1.03) | 0.95 (0.90-1.00) |
| Heterogeneity ($I^2$, *p-value*) | 0%, *p*=0.44 | 0%, *p*=0.42 | - | | | | 9.5%, *p*=0.36 | 18.5%, *p*=0.29 | 0%, *p*=0.96 |
| Egger's *p* value | - | - | - | | | | 0.72 | - | - |

[2]For dairy products we only had sufficient data to conduct individual analysis on total milk and cheese

* No data available

**1C** results of dose-response meta-analysis for alcohol, coffee, tea and legumes

| | 2005 SLR* | 2011 CUP SLR | | | 2015 CUP SLR | | |
|---|---|---|---|---|---|---|---|
| | | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Alcohol intake (as ethanol content)** | | | | | | | |
| Increment unit used | - | Per 10g/day | | | Per 10g/day | | |
| Studies (*n*) | | 8 | 12 | 11 | 16 | 14 | 11 |
| Cases (total number) | | 5261 | 7782 | 3584 | 15896 | 12051 | 7763 |
| Random effect RR (95%CI) | | 1.10 (1.06-1.13) | 1.08 (1.04-1.13) | 1.10 (1.07-1.12) | 1.07 (1.05-1.09) | 1.07 (1.05-1.09) | 1.08 (1.07-1.10) |
| Heterogeneity ($I^2$, *p-value)* | | 50.7%; *p*=0.05 | 60.1%, p≤0.01 | 0%, *p*=0.64 | 24.5%, *p*=0.21 | 34.2%, *p*=0.13 | 0%, *p*=0.54 |
| Egger's *p* value | | - | - | - | 0.33 | 0.24 | 0.07 |
| **Alcoholic Drinks** | | | | | | | |
| Increment unit used | - | 1 drink/day | | | 1 drink/day | | |
| Studies (n) | | 4 | 5 | 3 | 8 | 8 | 5 |
| Cases (total number) | | 1932 | 1460 | 353 | 36942 | 5207 | 963 |
| Random effect RR (95%CI) | | 1.11 (0.90-1.38) | 1.16 (0.97-1.39) | 1.11 (0.97-1.29) | 1.06 (1.00-1.11) | 1.11 (0.90-1.36) | 1.08 (1.00-1.17) |
| Heterogeneity ($I^2$, *p-value)* | | 76.6%, *p*=0.004 | 85.5% p<0.001 | 52.7%, *p*=0.12 | 60.4%, *p*=0.01 | 98.1%, p<0.001 | 62.2%, *p*=0.02 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Egger's p value | | 0.13 | 0.36 | 0.99 | 0.008 | 0.20 | 0.02 |

| | 2005 SLR | | | 2011 CUP SLR* | 2015 CUP SLR | | |
|---|---|---|---|---|---|---|---|
| | Colorectal cancer | Colon cancer | Rectal cancer | - | Colorectal cancer | Colon cancer | Rectal cancer |
| **Coffee** | | | | | | | |
| Increment unit | Highest vs. lowest | 1 cup/day | 1 cup/day | - | 1 cup/day | | |
| Studies (*n*) | 4 | 3 | 2 | | 14 | 11 | 15 |
| Cases (total number) | - | - | | | 20667 | 16688 | 7605 |
| Random effect RR (95%CI) | 0.96 (0.75-1.24) | 0.94 (0.88-1.01) | 0.97 (0.89-1.05) | | 1.00 (0.99-1.02) | 0.99 (0.97-1.01) | 1.01 (1.00-1.03) |
| Heterogeneity (*$I^2$, p-value)* | - | 0%, *p*=0.83 | 5.3%, *p*=0.35 | | 44.2%, *p*=0.05 | 48.8%, *p*=0.03 | 1.8%, *p*=0.43 |
| Egger's *p* value | - | - | - | | 0.002 | 0.55 | 0.73 |
| **Tea** | | | | | | | |
| Increment unit used | Highest vs. lowest | 1 cup/day | 1 cup/day | - | 1 cup/day | | |
| Studies (*n*) | 5 | 3 | 3 | | 8 | 6 | 9 |
| Cases (total number) | - | - | - | | 16 251 | 13 244 | 4 621 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Random effect RR (95%CI) | 1.01 (0.71-1.42) | 1.11 (0.92-1.34) | 0.94 (0.87-1.02) | | 0.99 (0.97-1.01) | 0.99 (0.94-1.03) | 0.99 (0.97-1.02) |
| Heterogeneity ($I^2$, *p-value*) | - | 83.1%, p =0.003 | 0%, *p*=0.56 | | 25.8%, *p*=0.23 | 75.1%, *p*=0.001 | 0%, *p*=0.47 |
| Egger's *p* value | - | - | - | | 0.42 | 0.33 | 0.04 |

| | 2005 SLR* | 2011 CUP SLR* | 2015 CUP SLR | | |
|---|---|---|---|---|---|
| | | | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Legumes** | | | | | |
| Increment unit used | - | - | 50g/day | | |
| Studies (*n*) | | | 4 | 6 | 4 |
| Cases (total number) | | | 7948 | 2145 | 729 |
| Random effect RR (95%CI) | | | 1.00 (0.95-1.06) | 0.97 (0.83-1.15) | 0.99 (0.78-1.25) |
| Heterogeneity (*$I^2$, p-value)* | | | 32.6%, *p*=0.20 | 55%, *p*=0.04 | 45.2%, *p*= 0.14 |
| Egger's *p* value | | | - | - | - |

* No data available

**1D** results of dose-response meta-analysis for meat, poultry and fish

| | **2005 SLR** | | | **2011 CUP SLR** | | | **2015 CUP SLR** | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer*** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Red and Processed meat** | | | | | | | | | |
| Increment unit | Highest vs. lowest | 100g/day | - | 100g/day | | | 100g/day | | |
| Studies (*n*) | 7 | 7 | - | 9 | 7 | 5 | 15 | 10 | 6 |
| Cases (total number) | - | - | - | 8894 | 5037 | 2091 | 31551 | 10010 | 3455 |
| Random effect RR (95%CI) | 1.24 (1.06-1.45) | 1.37 (1.10-1.70) | - | 1.16 (1.04-1.30) | 1.21 (1.06-1.39) | 1.31 (1.13-1.52) | 1.12 (1.04-1.21) | 1.19 (1.10-1.30) | 1.17 (0.99-1.39) |
| Heterogeneity ($I^2$, *p-value)* | 22.5%, *p*=0.26 | 61%, *p*=0.04 | - | 47%, *p*=0.06 | 56.0%, *p*=0.04 | 18.0%, *p*=0.30 | 70.2%, p<0.01 | 62.9%, *p*=0.004 | 48.4%, *p*=0.08 |
| Egger's *p* value | 0.70 | 0.69 | - | | | | 0.46 | 0.02 | 0.12 |
| **Processed meat** | | | | | | | | | |
| Increment unit used | 50g/day | Times/day | Highest vs. lowest | 50g/day | | | 50g/day | | |
| Studies (*n*) | 6 | 3 | 5 | 9 | 9 | 8 | 10 | 12 | 10 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cases (total number) | - | - | - | 10863 | 6338 | 2565 | 10738 | 8599 | 3029 |
| Random effect RR (95%CI) | 1.21 ( 1.04, 1.42) | 1.61 ( 1.13, 2.30) | 1.36 (1.03, 1.80) | 1.18 (1.10-1.28) | 1.24 (1.13-1.36) | 1.12 (0.99-1.28) | 1.16 (1.10-1.28) | 1.23 (1.11-1.35) | 1.08 (1.00-1.18) |
| Heterogeneity ($I^2$, *p-value*) | 25%, *p*=0.25 | 0%, *p*=0.97 | 25%, *p*=0.25 | 12%, *p*=0.33 | 0%, *p*=0.55 | 0%, *p*= 0.56 | 11%, *p*=0.34 | 26.2%, *p*=0.18 | 0%, *p*=0.77 |
| Egger's *p* value | 0.24 | - | - | | | | 0.29 | <0.01 | 0.61 |
| | **2005 SLR** | | | **2011 CUP SLR** | | | **2015 CUP SLR** | | |
| | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** | **Colorectal cancer** | **Colon cancer** | **Rectal cancer** |
| **Red meat** | | | | | | | | | |
| Increment unit used | 100g/day | | | 100g/day | | | 100g/day | | |
| Studies (*n*) | 5 | 9 | 5 | 8 | 9 | 7 | 8 | 11 | 8 |
| Cases (total number) | - | - | - | 4314 | 3172 | 1477 | 6662 | 4081 | 1772 |
| Random effect RR (95%CI) | 1.43 (1.05-1.94) | 1.34 ( 1.13, 1.60) | 1.35 (0.94-1.93) | 1.17 (1.05-1.31) | 1.12 0.97-1.29) | 1.18 (0.98-1.42) | 1.12 (1.00-1.25) | 1.22 (1.06-1.39) | 1.13 (0.96-1.34) |
| Heterogeneity ($I^2$, *p-value*) | 58.4%, *p*=0.01 | 15%, *p*=0.31 | 17.9%, *p*=0.30 | 0%, *p*=0.48 | 0%, *p*=0.89 | 0%, *p*=0.67 | 23.6%, *p*=0.24 | 11.7%, *p*=0.33 | 0%, *p*=0.52 |
| Egger's *p* value | 0.15 | 0.43 | 0.96 | | | | 0.48 | 0.76 | 0.45 |
| **Poultry** | | | | | | | | | |
| Increment unit used | 1 time/week | 1 time/week | Highest vs. lowest | - | | | 100g/day | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Studies (*n*) | 5 | 3 | 2 | | | | 7 | 10 | 6 |
| Cases (total number) | - | - | - | | | | 3429 | 8425 | 3201 |
| Random effect RR (95%CI) | 0.95 (0.90-1.01) | 1.10 (0.80-1.51) | 0.91 (0.70-1.19) | | | | 0.81 (0.53-1.25) | 0.83 (0.63-1.11) | 0.86 (0.72-1.01) |
| Heterogeneity *($I^2$, p-value)* | 25.2% *p*=0.25 | 0%, *p*=0.72 | - | | | | 48.0%, *p*=0.05 | 34.6%, *p*=0.12 | 0%, *p*=0.96 |
| Egger's *p* value | 0.89 | 0.98 | - | | | | 0.52 | 0.08 | 0.60 |
| **Fish** | | | | | | | | | |
| Increment unit used | 1 times/week | 1 times/week | Highest vs. lowest | 100g/day | | | 100g/day | | |
| Studies (*n*) | 9 | 4 | 4 | 9 | 10 | 7 | 11 | 11 | 10 |
| Cases (total number) | - | - | - | 4503 | 3156 | 1650 | 10356 | 10512 | 3944 |
| Random effect RR (95%CI) | 0.96 (0.92, 1.00) | 0.94 (0.90-1.08) | 0.84 (0.55-1.29) | 0.88 (0.74-1.06) | 0.90 (0.78-1.04) | 0.87 (0.69-1.10) | 0.89 (0.80-0.99) | 0.91 (0.80-1.03) | 0.84 (0.69-1.02) |
| Heterogeneity *($I^2$, p-value)* | 4.1%, *p*=0.4 | 0%, *p*=0.65 | 64.4%, *p*=0.04 | 38%, *p*=0.12 | 0%, 0.61 | 17%, *p*=0.30 | 0%, *p*=0.52 | 0%, *p*=0.76 | 14.7%, *p*=0.31 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Egger's *p* value | 0.98 | - | - | - | 0.39 | - | 0.27 | 0.32 | 0.56 |

* No data available

**Supplementary material**

Study selection

From 18860 articles retrieved by the search strategy and published between January 1st 2010 and May 30th 2015 identified, 13862 articles were excluded based on the abstract and title, 4447 articles did not meet the inclusion criteria and 551 articles met the inclusion criteria and, 233 articles were excluded because they did not report on food groups and beverages and colorectal cancer risk or because they were duplicated by another articles. After adding the relevant articles that were identified in the searches for the 2005 and 2010 WCRF SLR, a total of 111 articles were included in the review (Flowchart of study selection – Figure 1).

Statistical Methods

We calculated summary RRs and 95% CIs for the dose-response meta-analysis using random effect models to account for anticipated heterogeneity. The natural logarithm of the relative risks was weighted by the method of DerSimonian and Laird and then pooled across studies [3].To estimate linear trends and 95% CIs from the natural logs of the RR and respective CI across categories we used the method described by Greenland and Longnecker [4,5]. For this method at least three categories of intake and the number of cases and person-years or non-cases per category was required. When studies reported only the total number of cases or total person-years and the exposure was defined in quantiles, the distribution of cases or person-years was calculated dividing the total number by the number of quantiles. Whenever reported, the mean or median intake by category was assigned to the corresponding RR. The midpoint was calculated for studies that only reported a range of intake by category. When the intake range was open-ended we assumed that its width was the same as the adjacent category. The increment sizes used are comparable and equivalent to 1 standard deviation of intake.

Between-study heterogeneity was assessed using Cochran *Q* test and the percentage of total variation in study estimates attributable to between-study heterogeneity ($I^2$). Heterogeneity was explored in stratified analysis by sex and geographic location (see supplementary material on subgroup analysis). Low proportion of heterogeneity across studies was defined by an $I^2 < 30\%$, moderate proportion by an $I^2$ =30-50%, and high proportion by an $I^2 \geq 50\%$.

Small-study effects, such as publication bias, were explored using Egger's test in analysis with more than six studies. Influence analysis where we excluded one study at a time was conducted to investigate the robustness of the findings.

Study quality was not assessed by any score. Instead we looked at study characteristics such as study population, outcome assessment, dietary assessment methods and adjustment factors for each study.

Stata version 12 software (StataCorp, College Station, TX, USA) was used for the statistical analyses. A two-tailed $p<0.05$ was considered statistically significant.

**Subgroup analysis by exposure**

**Red and processed meats (Supplementary table 1)**

For colorectal cancer, the associations were similar in men (RR=1.10 (95%CI=1.02-1.18, $I^2$=0%, *ph*=0.66, 4 studies), and women (RR 1.13(95%CI=1.00-1.29, $I^2$=47%, *ph*=0.07, 8 studies).

In analysis stratified by geogra*ph*ic location, the results were significant for studies in Asia (RR=1.26(95%CI=1.16-1.36, $I^2$=0%, *ph*=0.83, 3 studies) and Europe (RR=1.09(95%CI=1.01-1.17 $I^2$=0%, *ph*=0.57, 3 studies) and not significant for North America RR=1.07(95%CI=0.95-1.20, $I^2$=77%, *ph*<0.01, 9 studies ), mostly because of one study with opposite results [39].

For colon cancer the association was significant in men (RR=1.32 (95%CI=1.13-1.53, $I^2$=28%, *ph*=0.66, 5 studies) but not in women (RR=1.18 (95%CI=0.98-1.43, $I^2$=44%, *ph*=0.07, 8 studies).

In the stratified analysis by geogra*ph*ic location the associations were of similar magnitude Asia (RR=1.23(95%CI=1.16-1.31, $I^2$=0%, *ph*=1.0, 3 studies) and Europe RR=1.26(95%CI=1.07-1.48 $I^2$=0%, 1 study) and less consistent for North America (RR=1.19(95%CI=0.98-1.38, $I^2$=68%, *ph*<0.01, 6 studies ), mostly because of two studies with opposite results [44,55].

**Processed meats (Supplementary table 1)**

A smaller number of studies could be included in the analysis of colorectal cancer stratified by sex. The summary relative risk of two studies in men was 1.11(95%CI=0.86-1.43, $I^2$=34%, *ph*=0.22) and for five studies in women the RR was 1.18 (95%CI=0.99-1.41, $I^2$=19%, *ph*=0.29).

In the stratified analysis by geogra*ph*ic location the results were significant for Europe RR=1.13(95%CI=1.03-1.24 $I^2$=0%, *ph*=0.74, 4 studies) or North America RR=1.20(95%CI=1.02-1.41, $I^2$=49%, *ph*=0.12, 4 studies).and not significant for Asia RR=1.37 (95%CI=0.76-2.49, $I^2$=31%, *ph*=0.23, 2 studies) or

For colon cancer, all stratified analysis by sex and geogra*ph*ic location were consistent showing statistically significant results. The exception was the subgroup analysis of Asian studies where the RR was 1.59(95%CI=0.93-2.71 $I^2$=43%, *ph*=0.15, 4 studies).

For rectal cancer, all stratified analysis by sex and geogra*ph*ic location showed non-significant results.

**Red meats (Supplementary table 1)**

For colorectal cancer a smaller number of studies could be included in the analysis stratified by sex. For men, only two studies were included and the RR was 1.28(95%CI=0.49-3.34 $I^2$=64%, *ph*=0.09), for women four studies were included and the RR was 1.02 (95%CI=0.78-1.33, $I^2$=11%, *ph*=0.34).

In the stratified analysis by geogra*ph*ic location the results were significant for Europe RR=1.20(95%CI=1.05-1.37 $I^2$=2%, *ph*=0.43, 6 studies) and not significant for Asia RR=1.03 (95%CI=0.71-1.49, $I^2$=48%, *ph*=0.16, 2 studies) or North America RR=1.01(95%CI=0.90-1.14, 1 study).

For colon cancer, for men the RR was 1.07(95%CI=0.74-1.56, 0%, *ph*=0.96, 2 studies) and for women RR was 1.14(95%CI=0.82-1.60, 39%, *ph*=0.13, 6 studies).

In the stratified analysis by geogra*ph*ic location the results were significant for Europe RR=1.38(95%CI=1.02-1.87 $I^2$=45%, *ph*=0.14, 3 studies) and not significant for Asia RR=1.14 (95%CI=0.90-1.44, $I^2$=18%, *ph*=0.31, 4 studies) or North America RR=1.13(95%CI=0.86-1.48, $I^2$=0%, *ph*=0.50, 4 studies).

For rectal cancer, all stratified analysis by sex and geogra*ph*ic location showed an overall non-significant result because of inconsistency in the direction of results of each individual study.

**Alcohol (Supplementary table 2)**

For colorectal cancer, the stratified analysis by sex showed an increases risk in men 1.08(95%CI=1.06-1.10, $I^2$=14%, *ph*=0.32, 14 studies) and a borderline significant increased risk in women 1.04 (95%CI=1.00-1.08, $I^2$=43%, *ph*=0.12, 10 studies). The subgroup analysis on women included a higher number of studies and the evidence of association was stronger than in the previous 2011 SLR CUP review (table 1). For colon cancer alcohol intake was associated with a significant increase in women (RR=1.06(95%CI=1.03-1.10, 0%, *ph*=0.46) and men (RR=1.08(95%CI=1.06-1.11, $I^2$=57%, *ph*=0.13). Rectal cancer was associated with an increased risk in men RR=1.07(95%CI=1.03-1.10, $I^2$=48%, *ph*=0.25) and women RR=1.09(95%CI=1.04-1.15, $I^2$=0%, *ph*=0.58).

For colorectal cancer, significant associations were observed in the analyses by geogra*ph*ic location; the heterogeneity was reduced but persisted within the threeNorth American studies RR=1.08 (95%CI=0.99-1.19, $I^2$=69%, *ph*=0.04, 3 studies). Low heterogeneity was observed for Asian studies RR=1.07 (95%CI=1.06-1.08, $I^2$=10%, *ph*=0.33, 7 studies) and no heterogeneity was observed for European studies RR=1.05 (95%CI=1.02-1.10, $I^2$=23%, *ph*=0.53, 5 studies).

For colon and rectal cancer the stratified analysis by geogra*ph*ic location were consistent. All subgroups showed a significant increase risk and no heterogeneity,.

**Wholegrains (Supplementary table 3)**

No stratified analysis by sex could be conducted.

Despite the small number of studies included, significant associations were observed in the analyses of colorectal stratified by geogra*ph*ic location, 11% decreased risk per 90g/day for European studies (RR=0.89 (95%CI=0.81-0.97, $I^2$=0%, *ph*=0.50, 2 studies) and 21% decreased risk for North American studies (RR= 0.79 (95%CI=0.72-0.86, $I^2$=0%, *ph*=0.57, 4 studies). No Asian studies were identified. There was insufficient data to conduct stratified analysis by geogra*ph*ic location for colon or rectal cancer.

**Total dairy products and milk (Supplementary table 4)**

For colorectal cancer similar associations were observed in men (RR=0.84;95%CI=0.80-0.89, 0%, p=0.69, 5 studies), women (RR=0.86;95%CI=0.78-0.96, 56%, p=0.05, 6 studies), European (RR=0.88 (95%CI=0.82-0.95, $I^2$=54%, *ph*=0.08, 5 studies) and North American studies (RR=0.85 (95%CI=0.80-0.89, $I^2$=0%, *ph*=0.90, 5 studies). No Asian studies were identified.

The same was observed for colon cancer. For men RR=0.77 (95%CI=0.68-0.88, $I^2$=0%, *ph*=0.61, 2 studies) and women RR= 0.98 (95%CI=0.87-1.11, $I^2$=0%, *ph*=0.81, 3 studies). For European studies RR=0.88 (0.82-0.95, $I^2$=54%, *ph*=0.07, 5 studies) and North American studies RR=0.85 (0.80-0.89, $I^2$= 0%, *ph*=0.90, 5 studies). Our dose-response analysis included only studies from Europe and North America because the only study from Asia identified [111] included only highest versus lowest results which were non-significant.

The association of milk intake with colorectal cancer was significant in men (RR=0.92 (95%CI=0.87-0.96, $I^2$=0%, p=0.96, 3 studies), but not in women (RR=0.96(95%CI=0.89-1.03, $I^2$=0% p=0.57, 4 studies). It was significant for European (RR=0.94 (95%CI=0.91-0.96, $I^2$=0%, *ph*=0.45, 5 studies) and North

American studies (RR=0.93 (95%CI=0.88-0.99, $I^2$=0%, *ph*=0.72, 3 studies). The only Asian study identified showed no association between milk intake and colorectal cancer risk [18].

For colon cancer the association was significant in men (RR=0.93 (95%CI=0.88-0.98, $I^2$=41%, p=0.15, 5 studies), but not in women (RR=0.98(95%CI=0.89-1.09, $I^2$=32% p=0.22, 4 studies). No stratified analysis by geogra*ph*ic location was conducted.
For rectal cancer the association was significant in women (RR=0.93 (95%CI=0.88-0.98, $I^2$=0%, p=0.94, 5 studies) but not in men (RR=0.91(95%CI=0.83-1.09, $I^2$=0% p=0.76, 3 studies). No stratified analysis by geogra*ph*ic location was conducted.

**Vegetables (Supplementary table 5)**

For both colorectal and colon cancer the association remained significant in men but not in women. For colorectal cancer the RR for men was 0.96(95%CI=0.93-0.99, $I^2$=33%, *ph*=0.21, 5 studies) and for women 0.99 (95%CI=0.96-1.01, $I^2$=0%, *ph*=0.83, 7 studies). For colon cancer the RR for men was 0.95(95%CI=0.92-0.99, $I^2$=0%, *ph*=0.48, 6studies) and for women 0.99(95%CI=0.95-1.03, $I^2$=0%, *ph*=0.73, 6 studies).

For colorectal cancer the stratified analysis by geogra*ph*ic location showed a non-significant association for the different subgroups:  Asia (RR=0.87 (95%CI=0.77-0.98, 1 study), Europe (RR=0.99 (95%CI=0.95-1.03, $I^2$=0%, *ph*=0.56, 3 studies) and North America (RR= 0.98 (95%CI=0.96-0.99, $I^2$=0%, *ph*=0.66, 7 studies).No stratified analysis by geogra*ph*ic location was conducted for colon or rectal cancer.

**Fish (Supplementary table 6)**

For colorectal cancer the association remained significant in men (RR=0.83(0.71-0.98, $I^2$=11%, *ph*=0.34, 6 studies), but not in women (RR=0.96 (0.82-1.12, $I^2$=0%, *ph*=0.53, 7 studies).

The stratified analysis by geogra*ph*ic location showed a non-significant association for the different subgroups:  Asia (RR=1.03 (95%CI=0.84-1.26, $I^2$=0%, *ph*=0.90, 3 studies), Europe (RR=0.85 (95%CI=0.71-1.01), $I^2$=2%, *ph*=0.38, 4 studies) and North America (RR=0.83 (95%CI=0.68-1.03) $I^2$=0.5%, *ph*=0.39, 4 studies).

## Mechanisms

For most of the food groups analysed there are plausible mechanisms that explain the association with colorectal cancer. Further discuss of the mechanisms is included in the supplementary material section. There are several potential underlying mechanisms for a positive association of red and processed meat consumption with colorectal cancer. Red meat contains haem, which promotes the formation of potentially carcinogenic N-nitroso compounds as well as cytotoxic alkenals formed from fat peroxidation. The formation of N-nitroso compounds is particularly important when nitrate or nitrite is added as a preservative. [118].

Several mechanisms have been studied to explain the association between alcohol and colorectal cancer. Acetaldehyde, the reactive metabolite of alcohol, is carcinogenic to humans. Alcohol also acts as a solvent, enhancing penetration of carcinogens into cells[119]. Alcohol has been demonstrated to interfere with retinoid metabolism, which may adversely affect cellular growth, cellular differentiation and apoptosis [120]. For all these pathways, genetic polymor*ph*isms might also influence risk. There is also an interaction with smoking. Tobacco may induce specific mutations in DNA that are less efficiently repaired in the presence of alcohol.

The benefit of whole grains may manily be related to the content of fibre of these foods. The precise mechanism by which fibre is protective is not clearly understood. [114,115]. The studies on different sources of dietary fiber in general find stronger associations of cereal fiber as compared with other fiber sources (e.g. legumes, vegetables, fruits). This may be due to the types of fiber found in cereals, but it could also be due to other health beneficial compounds found together with the fibers in the bran (e.g. lignans, minerals etc.)

As part of the analysis of the 2015 CUP SLR, after including the results of the Pooling Project [112], we observed a borderline significant 7% decrease risk of colorectal cancer RR per 10g/day dietary fibre=0.93 (95%CI=0.87-1.00, 72%, *ph*<0.001, 21 studies, 16 562 cases).

The study by Kyrø et al. included 1372 incident colorectal cancer patients and 1372 individual matched control subjects from the EPIC study. Alkylresorcinol concentrations were measured in prediagnostic plasma samples as an objective measure of whole-grain wheat and rye intake. The authors found that a high plasma total alkylresorcinol concentration was associated with a statistically significant lower incidence of distal colon cancer after adjustment for other colorectal cancer risk factors, including dietary folate intake (relative risk = 0.53; 95% confidence interval = 0.30 to 0.93, for highest vs lowest quartile) [116,117].

It is hard to dissociate the mechanism of fruits and vegetables. This is a wide food category, and many different plant food constituents could feasibly contribute to a protective effect of non-starchy vegetables. These include dietary fibre, carotenoids, folate, selenium, glucosinolates, dithiolthiones, indoles, coumarins, ascorbate, chloro*ph*yll, flavonoids, allylsul*ph*ides, flavonoids, and *ph*ytoestrogens. Antioxidants, one of the multiple potential mechanisms, trap free radicals and reactive oxygen molecules, protecting against oxidation damage [106,121].

Most mechanisms identified for fish are general and not colorectal-specific. It is biologically plausible that long-chain n-3 polyunsaturated fatty acids (PUFAs) found in fish protect against cancer [122]. Fish oils reduce tumours in animal studies. This mechanism, though plausible, is not well supported. [122].

As part of the analysis of the 2015 CUP SLR per 0.3g/day of n-3 fatty acids from fish we observed a not-significant association for colorectal cancer RR=1.02 (95%CI=0.96-1.09, $I^2$=0%, *ph*=0.88, 5 studies, 3647 cases).

The result for total dairy product intake may largely be driven by an effect of milk intake, as milk accounts for a large part of total dairy intakes in most populations. Any effect of milk in reducing colorectal cancer risk is likely to be mediated at least in part by calcium, which restrains cellular proliferation and promotes differentiation and apoptosis in normal and tumour colorectal cells. In this review we included only analysis on foods and not on micronutrients. However as part of the 2015 CUP SLR the analysis per 200mg/day of dietary calcium showed a 6% decrease risk in colorectal cancer, RR=0.94 (95%CI=0.93-0.96, $I^2$=0%, 13 studies).

Supplementary table 1 – Subgroup analysis on red and processed meat

**Red and processed meat**

| | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 100g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 1.10 (1.02-1.18) | 0% | 4 | 1.32 (1.13-1.53) | 28% | 5 | 0.92 (0.59-1.42) | - | 1 |
| **Women** | 1.13 (1.00-1.29) | 47% | 8 | 1.18 (0.98-1.43) | 44% | 8 | 1.34 (0.85-2.11) | 47% | 3 |
| **Asia** | 1.26 (1.16-1.36) | 0% | 3 | 1.23 (1.16-1.31) | 0% | 3 | 0.93 (0.64-1.33) | - | 1 |
| **Europe** | 1.09 (1.01-1.17) | 0% | 3 | 1.26 (1.07-1.48) | - | 1 | 1.23 (1.01-1.50) | 0% | 2 |
| **N. America** | 1.07 (0.95-1.20) | 77% | 9 | 1.19 (0.98-1.38) | 68% | 6 | 1.33 (0.91-1.96) | 74% | 3 |

**Processed meat**

| | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 50g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 1.11 (0.86-1.43) | 34% | 2 | 1.58 (1.11-2.23) | 50% | 5 | 0.82 (0.52-1.29) | 0% | 3 |
| **Women** | 1.18 (0.99-1.41) | 19% | 5 | 1.32 (1.13-1.55) | 0% | 8 | 1.12 (0.86-1.46) | 0% | 5 |
| **Asia** | 1.37 (0.76-2.49) | 31% | 2 | 1.59 (0.93-2.71) | 43% | 4 | 1.25 (0.64-2.45) | 28% | 3 |
| **Europe** | 1.13 (1.03-1.24) | 0% | 4 | 1.19 (1.05-1.35) | 0% | 3 | 1.08 (0.92-1.26) | 0% | 3 |
| **N. America** | 1.20 (1.02-1.41) | 21% | 4 | 1.14 (1.06-1.23) | 3% | 5 | 1.08 (0.98-1.19) | 0% | 3 |

**Red meat**

| | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 100g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 1.28 (0.49-3.34) | 64% | 2 | 1.07 (0.74-1.56) | 0% | 2 | 0.90 (0.92-1-92) | - | 1 |
| **Women** | 1.02 (0.78-1.33) | 11% | 4 | 1.14 (0.82-1.60) | 39% | 6 | 0.86 (0.58-1.27) | 0% | 4 |
| **Asia** | 1.03 (0.71-1.49) | 48% | 2 | 1.14 (0.90-1.44) | 18% | 4 | 1.10 (0.74-1.64) | 45% | 3 |
| **Europe** | 1.20 (1.05-1.37) | 2% | 6 | 1.38 (1.02-1-87) | 45% | 3 | 1.19 (0.95-1.50) | 0% | 3 |
| **N. America** | 1.01 (0.90-1.14) | - | 1 | 1.13 (0.86-1.48) | 0% | 4 | 0.89 (0.51-1.56) | 0% | 2 |

Supplementary table 2 – Subgroup analysis on alcohol as ethanol

| **Alcohol as ethanol** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal** | | | **Colon** | | | **Rectal** | | |
| **Per 10g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 1.08 (1.06-1.10) | 13.9% | 14 | 1.08 (1.06-1.11) | 56.7%, | 12 | 1.09 (1.06-1.12) | 25%, | 10 |
| **Women** | 1.04 (1.00-1.08) | 42.9% | 10 | 1.05 (1.02-1.09) | 0% | 10 | 1.09 (1.04-1.15) | 0% | 8 |
| **Asia** | 1.07 (1.06-1.08) | 10.7% | 7 | 1.08 (1.07-1.10) | 0% | 8 | 1.07 (1.05-1.10) | 0% | 7 |
| **Europe** | 1.05 (1.01-1.10) | 22.7% | 5 | 1.04 (1.01-1.07) | 0% | 3 | 1.09 (1.05-1.12) | 0% | 3 |
| **N. America** | 1.08 (0.99-1.19) | 68.6% | 3 | 1.14 (0.98-1.32) | 62.1% | 3 | 1.03 (1.01-1.04) | - | 1 |

Supplementary table 3 – Subgroup analysis on wholegrains

| **Wholegrains** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Colorectal** | | | **Colon** | | | **Rectal** | | |
| **Per 90g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | - | - | - | - | - | - | - | - | - |
| **Women** | - | - | - | - | - | - | - | - | - |
| **Asia** | - | - | - | - | - | - | - | - | - |
| **Europe** | 0.89 (0.81-0.97 | 0% | 2 | - | - | - | - | - | - |
| **N. America** | 0.79 (0.72-0.86) | 0% | 4 | - | - | - | - | - | - |

Supplementary table 4 – Subgroup analysis on dairy products and milk

**Dairy products**

| | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 400 g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 0.84 (0.80-0.89) | 0% | 5 | 0.77 (0.68-0.88) | 0% | 2 | - | - | - |
| **Women** | 0.86 (0.78-0.96) | 55.7% | 6 | 0.98 (0.87-1.11) | 0% | 3 | - | - | - |
| **Asia** | - | - | - | - | - | - | - | - | - |
| **Europe** | 0.88 (0.82-0.95) | 53.8% | 5 | - | - | - | - | - | - |
| **N. America** | 0.85 (0.80-0.89) | 0% | 5 | - | - | - | - | - | - |

**Milk**

| | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **per 200 g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 0.92 (0.87-0.98) | 0% | 3 | 0.93 (0.88-0.98) | 41.4% | 5 | 0.91 (0.83-1.00) | 0% | 3 |
| **Women** | 0.96 (0.89-1.03) | 0% | 4 | 0.98 (0.89-1.09) | 31.6% | 4 | 0.93 (0.88-0.98) | 0% | 3 |
| **Asia** | 0.81 (0.59-1.10) | 0% | 1 | - | - | - | - | - | - |
| **Europe** | 0.94 (0.91-0.96) | 0% | 5 | - | - | - | - | - | - |
| **N. America** | 0.93 (0.88-0.99) | 0% | 3 | - | - | - | - | - | - |

Supplementary table 5 – Subgroup analysis on vegetables

| Vegetables | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 100g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 0.96 (0.93-0.99) | 33% | 5 | 0.95 (0.92-0.99) | 0% | 6 | 0.96 (0.91-1.01) | 0% | 4 |
| **Women** | 0.99 (0.96-1.01) | 0% | 7 | 0.99 (0.95-1.03) | 0% | 6 | 1.00 (0.93-1.08) | 24% | 4 |
| **Asia** | 0.87 (0.77-0.98) | - | 1 | - | - | - | - | - | - |
| **Europe** | 0.99 (0.95-1.03) | 0% | 3 | - | - | - | - | - | - |
| **N. America** | 0.98 (0.96-0.99) | 0% | 7 | - | - | - | - | - | - |

Supplementary table 6 – Subgroup analysis on fish

| Fish | Colorectal | | | Colon | | | Rectal | | |
|---|---|---|---|---|---|---|---|---|---|
| **Per 100g/day** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** | **RR (95% CI)** | $I^2$ | **No. of studies** |
| **Men** | 0.83 (0.71-0.98) | 11% | 6 | 1.09 (0.86-1.38) | 0% | 4 | 0.88 (0.50-1.55) | 64% | 3 |
| **Women** | 0.96 (0.82-1.12) | 0% | 7 | 0.94 (0.72-1.22) | 0% | 7 | 0.95 (0.65-1.41) | 0% | 5 |
| **Asia** | 1.03 (0.84-1.26) | 0% | 3 | 1.04 (0.85-1.28) | 0% | 4 | 1.04 (0.80-1.35) | 0% | 4 |
| **Europe** | 0.85 (0.71-1.01) | 2% | 4 | 0.74 (0.58-0.93) | 0% | 3 | 0.64 (0.46-0.88) | 0% | 3 |
| **N. America** | 0.83 (0.68-1.03) | 0.5% | 4 | 0.91 (0.74-1.13) | 0% | 4 | 0.70 (0.43-1.16) | 33% | 3 |
| **Adjusted for meat Yes** | 0.89 (0.79-1.01) | 9% | 7 | 0.98 (0.84-1.14) | 0% | 6 | 0.95 (0.77-1.17) | 0% | 7 |
| **Adjusted for meat No** | 0.94 (0.66-1.34) | 0% | 4 | 0.76 (0.61-0.95) | 0% | 5 | 0.64 (0.47-0.87) | 0% | 3 |