# **Supplementary Materials**

Journal name: Nutrients

Title: Effect of red, processed, and white meat consumption on the risk of gastric cancer: An overall and dose-response meta-analysis

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#### Table S1. PRISMA 2009 Checklist

| Section/topic             | #  | Checklist item  | Reported<br>on page # |
|---------------------------|----|---|-----------------------|
| TITLE                     |    |   |                       |
| Title                     | 1  | Identify the report as a systematic review, meta-analysis, or both.   | 1                     |
| ABSTRACT                  |    |   |                       |
| Structured summary        | 2  | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 1                     |
| INTRODUCTION              | -  |   |                       |
| Rationale                 | 3  | Describe the rationale for the review in the context of what is already known.  | 1-2                   |
| Objectives                | 4  | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).  | 2                     |
| METHODS                   |    |   |                       |
| Protocol and registration | 5  | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.   | NA                    |
| Eligibility criteria      | 6  | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.  | 2, 11-12              |
| Information sources       | 7  | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.  | 2, 11-12              |
| Search                    | 8  | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.   | 2, 11-12              |
| Study selection           | 9  | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).   | 2, 11-12              |
| Data collection process   | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.  | 2, 11-12              |

| Data items                         | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.  | 2, 11-12 |
|------------------------------------|----|--|----------|
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 2, 11-12 |
| Summary measures                   | 13 | State the principal summary measures (e.g., risk ratio, difference in means).  | 2, 11-12 |
| Synthesis of results               | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis.   | 2, 11-12 |

| Section/topic                 | #  | Checklist item   | Reported<br>on page # |
|-------------------------------|----|--|-----------------------|
| Risk of bias across studies   | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).   | 2, 11-12              |
| Additional analyses           | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.   | 2, 11-12              |
| RESULTS                       |    |  |                       |
| Study selection               | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.  | 11-24                 |
| Study characteristics         | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.   | 11-24                 |
| Risk of bias within studies   | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).  | 11-24                 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 11-24                 |
| Synthesis of results          | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency.  | 11-24                 |
| Risk of bias across studies   | 22 | Present results of any assessment of risk of bias across studies (see Item 15).  | 11-24                 |
| Additional analysis           | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).  | 11-24                 |
| DISCUSSION                    |    |  |                       |

| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 24-26 |
|---------------------|----|--|-------|
| Limitations         | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).                        | 24-26 |
| Conclusions         | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research.  | 26    |
| FUNDING             |    |  |       |
| Funding             | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.   | 26    |

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

### Table S2. Search terms

| MEDLINE (PubMed) | ("meat"[tw] OR "meats"[tiab] OR "meat product"[tiab] OR "meat products"[tw] OR "red meat"[tw] OR "red meats"[tiab] OR beef[tiab]    |
|------------------|---|
|                  | OR veal[tiab] OR goat[tiab] OR lamb[tiab] OR pork[tiab] OR mutton[tiab] OR sausage[tiab] OR sausages[tiab] OR ham[tiab] OR          |
|                  | hams[tiab] OR pastrami[tiab] OR bacon[tiab] OR bacons[tiab] OR salami[tiab] OR salamis[tiab] OR "hot dog"[tiab] OR "hot dogs"[tiab] |
|                  | OR "animal food"[tiab] OR "animal foods"[tiab] OR "animal protein"[tiab] OR "animal proteins"[tiab] OR diet[tiab] OR diets[tiab] OR |
|                  | dietary[tiab] OR "white meat"[tiab] OR "poultry"[tiab] OR "chicken"[tiab] OR "duck"[tiab] OR "turkey"[tiab] OR "rabbit"[tiab]) AND  |
|                  | ("gastric cancer"[tiab] OR "gastric neoplasm"[tiab] OR "stomach cancer"[tiab] OR "stomach neoplasm"[tiab] OR "gastric               |
|                  | malignancy"[tiab] OR "stomach malignancy"[tiab] OR "gastric tumor"[tiab] OR "stomach tumor"[tiab])                                  |
| EMBASE           | ("meat" OR "meats" OR "meat product" OR "meat products" OR "red meat" OR "red meats" OR beef OR veal OR goat OR lamb OR             |
| Cochrane Library | pork OR mutton OR sausage OR sausages OR ham OR hams OR pastrami OR bacon OR bacons OR salami OR salamis OR "hot dog"               |
|                  | OR "hot dogs" OR "animal food" OR "animal foods" OR "animal protein" OR "animal proteins" OR "diet" OR "diets" OR "dietary" OR      |
|                  | "white meat" OR "poultry" OR "chicken" OR "duck" OR "turkey" OR "rabbit") AND ("gastric cancer" OR "gastric neoplasm" OR            |
|                  | "stomach cancer" OR "stomach neoplasm" OR "gastric malignancy" OR "stomach malignancy" OR "gastric tumor" OR "stomach               |
|                  | tumor")   |

|               | 1 1                   | ,                |               | ,                    | ·                     |            |                                    |                      |               |
|---------------|-----------------------|------------------|---------------|----------------------|-----------------------|------------|------------------------------------|----------------------|---------------|
| First author, | Representativeness of | Selection of the | Ascertainment | Outcome of interest  | Control for important | Outcome    | Follow-up long enough              | Adequacy of          | Total quality |
| year          | the exposed cohort    | unexposed        | of exposure   | not present at start | factor or additional  | assessment | for outcomes to occur <sup>c</sup> | follow-up of         | scores        |
|               |                       | cohort           |               | of study             | factors <sup>b</sup>  |            |                                    | cohorts <sup>d</sup> |               |
| Nomura A,     | ☆                     | ☆                | ☆             | ☆                    | **                    | ☆          | ☆                                  | -                    | 8             |
| 1990          |                       |                  |               |                      |                       |            |                                    |                      |               |
| Zheng, 1995   | ☆                     | ☆                | ☆             | ☆                    | **                    | ☆          | *                                  | ☆                    | 9             |
| Galanis D J,  | ☆                     | ☆                | ☆             | ☆                    | ☆                     | ☆          | ☆                                  | 4                    | 8             |
| 1998          |                       |                  |               |                      |                       |            |                                    |                      |               |
| Knekt P, 1999 | ☆                     | ☆                | ☆             | ☆                    | **                    | ☆          | ☆                                  | ☆                    | 9             |
| Huang, 2000   | ☆                     | ☆                | ☆             | ☆                    | **                    | ☆          | ☆                                  | ☆                    | 9             |
| González CA,  | ☆                     | ☆                | -             | ☆                    | **                    | ☆          | ☆                                  | \$                   | 8             |
| 2006          |                       |                  |               |                      |                       |            |                                    |                      |               |
| Larsson SC,   | ☆                     | ☆                | ☆             | ☆                    | ☆☆                    | *          | ☆                                  | ☆                    | 9             |
| 2006          |                       |                  |               |                      |                       |            |                                    |                      |               |
| Cross AJ,     | ☆                     | ☆                | ☆             | ☆                    | ☆☆                    | *          | ☆                                  | ☆                    | 9             |
| 2011          |                       |                  |               |                      |                       |            |                                    |                      |               |
| Daniel        | ☆                     | ☆                | *             | ☆                    | **                    | ☆          | *                                  | ☆                    | 9             |
| Keszei AP,    | ☆                     | ☆                | ☆             | ☆                    | **                    | *          | \$                                 | ☆                    | 9             |
| 2012          |                       |                  |               |                      |                       |            |                                    |                      |               |
| 1             |                       | 1                | 1             |                      |                       | 1          |                                    | 1                    |               |

#### Table S3. The quality of cohort studies (Newcastle-Ottawa Scale) included in the meta-analysis <sup>a</sup>

| Wie, 2014 | ☆ | ☆ | ☆ | ☆ | ☆☆ | * | - | ☆ | 8 |
|-----------|---|---|---|---|----|---|---|---|---|
|           |   |   |   |   |    |   |   |   |   |

a. A maximum of one star was assigned for almost all of the items.

b. A maximum of two stars was assigned for this item. Studies that adjusted for age received one star, whereas studies that adjusted for other important confounders additionally such as family history

of cancer or helicobacter pylori infection or health behaviors (such as smoking or alcohol drinking) received an additional star.

c. A cohort study with a follow-up period >8 y was assigned one star.

d. A cohort study with a follow-up rate >75% was assigned one star.

| First author, | Adequate definition | Representativeness | Selection of | Definition of | Control for important | Exposure   | Same method of        | Nonresponse       | Total quality |
|---------------|---------------------|--------------------|--------------|---------------|-----------------------|------------|-----------------------|-------------------|---------------|
| year          | of cases            | of cases           | controls     | controls      | factor or additional  | assessment | ascertainment for all | rate <sup>c</sup> | scores        |
|               |                     |                    |              |               | factors <sup>b</sup>  |            | subjects              |                   |               |
| Lee HH, 1990  | *                   | \$                 | -            | -             | *                     | -          | *                     | -                 | 4             |
| Boeing H,     | -                   | ☆                  | -            | ☆             | **                    | -          | \$                    | -                 | 5             |
| 1991          |                     |                    |              |               |                       |            |                       |                   |               |
| González CA,  | ☆                   | ☆                  | -            | ☆             | ☆                     | ☆          | *                     | -                 | 6             |
| 1991          |                     |                    |              |               |                       |            |                       |                   |               |
| Hoshiyama Y,  | ☆                   | ☆                  | ☆            | ☆             | **                    | ☆          | ☆                     | -                 | 8             |
| 1992          |                     |                    |              |               |                       |            |                       |                   |               |
| Muñoz SE,     | ☆                   | ☆                  | -            | ☆             | ☆                     | ☆          | ☆                     | -                 | 6             |
| 1997          |                     |                    |              |               |                       |            |                       |                   |               |
| Ward MH,      | ☆                   | ☆                  | ☆            | ☆             | ☆                     | ☆          | *                     | -                 | 7             |
| 1997          |                     |                    |              |               |                       |            |                       |                   |               |
| Ji BT, 1998   | *                   | \$                 | ☆            | -             | **                    | ☆          | \$                    | -                 | 7             |
| Ward MH,      | ☆                   | ☆                  | ☆            | -             | **                    | *          | ☆                     | -                 | 7             |
| 1999          |                     |                    |              |               |                       |            |                       |                   |               |
| Tavani A,     | ☆                   | ☆                  | -            | ☆             | ☆☆                    | ☆          | ☆                     | -                 | 7             |
| 2000          |                     |                    |              |               |                       |            |                       |                   |               |
| Takezaki T,   | ☆                   | ☆                  | ☆            | -             | ☆☆                    | ☆          | ☆                     | -                 | 7             |

## Table S4. The quality of case-control studies (Newcastle-Ottawa Scale) included in the meta-analysis <sup>a</sup>

| 2001                           |    |   |    |    |                 |   |    |   |   |
|--------------------------------|----|---|----|----|-----------------|---|----|---|---|
| Palli D, 2001                  | *  | * | ☆  | -  | **              | ☆ | \$ | - | 7 |
| Kim HJ, 2002                   | \$ | * | -  | \$ | **              | ☆ | \$ | - | 7 |
| Ito LS, 2003                   | *  | ☆ | -  | \$ | **              | ☆ | \$ | - | 7 |
| Nomura AM,<br>2003             | \$ | * | \$ | -  | **              | ☆ | *  | - | 7 |
| Lissowska J,<br>2004           | \$ | * | \$ | -  | **              | * | \$ | - | 7 |
| De Stefani E,<br>2004          | \$ | * | -  | \$ | **              | * | \$ | - | 7 |
| Phukan RK,<br>2006             | *  | * | -  | \$ | <b>☆</b>        | * | ☆  | - | 6 |
| Strumylaitė<br>L, 2006         | \$ | * | -  | -  | \$              | * | \$ | - | 5 |
| Wu AH,<br>2007, USA            | \$ | * | \$ | \$ | **              | * | *  | * | 9 |
| Navarro<br>Silvera SA,<br>2008 | \$ | * | \$ | -  | **              | * | \$ | - | 7 |
| Hu JF, 2008                    | ☆  | ☆ | ☆  | -  | $\Delta \Delta$ | ☆ | ☆  | - | 7 |

| Aune D, 2009  | ☆  | ☆ | - | *  | ☆☆ | ☆ | \$ | - | 7 |
|---------------|----|---|---|----|----|---|----|---|---|
| Aune D, 2009  | ☆  | * | - | ☆  | ☆☆ | ☆ | \$ | - | 7 |
| Pourfarzi E,  | ☆  | ☆ | ☆ | ☆  | ** | ☆ | \$ | - | 8 |
| 2009          |    |   |   |    |    |   |    |   |   |
| Gao Y, 2011,  | ☆  | ☆ | - | ☆  | ☆  | ☆ | \$ | * | 7 |
| China         |    |   |   |    |    |   |    |   |   |
| Hu, 2011      | ☆  | ☆ | ☆ | ☆  | ** | ☆ | \$ | - | 8 |
| De Stefani,   | ☆  | ☆ | - | ☆  | ** | ☆ | \$ | ☆ | 8 |
| 2012          |    |   |   |    |    |   |    |   |   |
| Wang, 2012    | ☆  | * | ☆ | ☆  | *  | ☆ | \$ | - | 7 |
| Di maso,      | ☆  | ☆ | ☆ | -  | ☆☆ | - | ☆  | - | 6 |
| 2013          |    |   |   |    |    |   |    |   |   |
| Zamani, 2013  | ☆  | * | ☆ | *  | ☆☆ | ☆ | 4  | - | 8 |
| Epplein, 2014 | ☆  | * | ☆ | ☆  | ☆☆ | ☆ | \$ | - | 8 |
| Lin, 2014     | ☆  | ☆ | - | \$ | ** | ☆ | \$ | - | 7 |
| Ellison-      | \$ | ☆ | ☆ | -  | ** | ☆ | \$ | - | 7 |
| Loschmann,    |    |   |   |    |    |   |    |   |   |
| 2017          |    |   |   |    |    |   |    |   |   |

a. A maximum of one star was assigned for almost all of the items.

b. A maximum of two stars was assigned for this item. Studies that adjusted for age received one star, whereas studies that adjusted for other important confounders additionally such as family history

of cancer or helicobacter pylori infection or health behaviors (such as smoking or alcohol drinking) received an additional star.

c. A maximum of one star was assigned for this item if there was no significant difference in the response rate between cases and controls by using the chi-square test (P>0.05)



Figure S1. Comparison of the adjusted relative risks and 95% confidence intervals of gastric cancer for the highest versus lowest groups of red meat consumption (studies included for the dose-response analysis versus studies not included for the dose-response analysis). Squares mean each study's relative risks. Horizontal lines mean 95% confidence intervals. Diamonds mean the summary relative risks and 95% confidence intervals.

| ID   | RR (95% CI)               | Weight |
|--|---------------------------|--------|
| Included                                       |                           |        |
| Nomura, 1990                                   | 1.30 (0.90, 2.00)         | 4.06   |
| Zheng, 1995                                    | 2.20 (0.80, 6.00)         | 1.45   |
| Galanis (M), 1998                              | 1.00 (0.50, 1.90)         | 2.54   |
| Galanis (W), 1998                              | 1.20 (0.60, 2.40)         | 2.43   |
| Gonzalez, 2006                                 | 1.62 (1.08, 2.41)         | 4.05   |
| arsson 2006                                    | 1 66 (1 13, 2 45)         | 4 14   |
| Cross. 2011                                    | 1.09 (0.81, 1.48)         | 4.74   |
| Keszei (M), 2012                               | 1.19 (0.78, 1.79)         | 3.95   |
| Keszei (W) 2012                                | 1 11 (0 73 1 70)          | 3.90   |
| Ward 1997                                      | 1 60 (0 90, 2 90)         | 2.93   |
| Ward 1999                                      | 3 20 (1 50, 6 60)         | 2 24   |
| Takezaki 2001                                  | 2 36 (1.08, 5.14)         | 2.09   |
| Nomura (M) 2003                                | 1 70 (0 90, 3 30)         | 2.62   |
| Nomura (W) 2003                                | 0.70 (0.30, 1.50)         | 2.01   |
|  | 1 23 (0 79 1 93)          | 3 75   |
| Pkukan 2006                                    | 2 80 (1 70, 8 80)         | 1 95   |
| Strumylaite 2006                               | 2 21 (1 43 3 42)          | 3.81   |
|  | 1.62(1.07, 2.44)          | 3.97   |
| Aune, 2009                                     | 4 39 (2 17 8 90)          | 2.37   |
| Hu 2011  | 1 70 (1 30, 2 20)         | 5.01   |
| Lin 2014                                       | <b>5</b> 95 (1 33, 25 62) | 0.77   |
| Subtotal (I-squared = $48.5\%$ , p = 0.007)    | 1.57 (1.34, 1.84)         | 64.79  |
|  |                           |        |
| Excluded                                       |                           |        |
| Knekt, 1999                                    | 0.49 (0.22, 1.06)         | 2.07   |
| Lee, 1990                                      | - 2.31 (1.30, 4.00)       | 3.06   |
| Boeing, 1991                                   | 2.21 (1.32, 3.71)         | 3.31   |
| Gonzalez, 1991                                 | 1.40 (0.67, 1.44)         | 4.17   |
| Hoshiyama, 1992                                | 1.40 (0.90, 2.40)         | 3.47   |
| Hoshiyama, 1992                                | 1.90 (1.00, 3.30)         | 2.87   |
| Palli, 2001                                    | 1.00 (0.40, 2.60)         | 1.62   |
| lto, 2003                                      | 0.50 (0.22, 1.13)         | 1.96   |
| Wu, 2007                                       | 1.65 (1.10, 2.50)         | 3.98   |
| Pourfarzi, 2009                                | 1.14 (0.55, 2.37)         | 2.28   |
| De Stefani(M), 2012                            | 1.93 (1.25, 2.98)         | 3.83   |
| De Stefani(W), 2012                            | 4.51 (2.34, 8.70)         | 2.59   |
| Subtotal (I-squared = 66.4%, p = 0.001)        | 1.52 (1.15, 2.02)         | 35.21  |
| Overall (I-squared = 55.5%, p = 0.000)         | 1.57 (1.37, 1.81)         | 100.00 |
| NOTE: Weights are from random effects analysis |                           |        |

Figure S2. Comparison of the adjusted relative risks and 95% confidence intervals of gastric cancer for the highest versus lowest groups of processed meat consumption (studies included for the dose-response analysis). Squares mean each study's relative risks. Horizontal lines mean 95% confidence intervals. Diamonds mean the summary relative risks and 95% confidence intervals.



Figure S3. Comparison of the adjusted relative risks and 95% confidence intervals of gastric cancer for the highest versus lowest groups of white meat consumption (studies included for the dose-response analysis versus studies not included for the dose-response analysis). Squares mean each study's relative risks. Horizontal lines mean 95% confidence intervals. Diamonds mean the summary relative risks and 95% confidence intervals.

### a. Highest versus lowest categories



Begg's funnel plot with pseudo 95% confidence limits

# b. Red meat (per 100g/day)

Begg's funnel plot with pseudo 95% confidence limits



Figure S4. Begg's funnel plot of studies for red meat consumption and gastric cancer risk. (a) Funnel plot of the highest versus lowest categories of red meat consumption and gastric cancer risk.; (b) Funnel plot of 100g/day increase in red meat consumption and gastric cancer risk.

### a. Highest versus lowest categories



Begg's funnel plot with pseudo 95% confidence limits

#### b. Processed meat (per 50g/day)

Begg's funnel plot with pseudo 95% confidence limits



Figure S5. Begg's funnel plot of studies for processed meat consumption and gastric cancer risk. (a) Funnel plot of the highest versus lowest categories of processed meat consumption and gastric cancer risk.; (b) Funnel plot of 100g/day increase in processed meat consumption and gastric cancer risk.

### a. Highest versus lowest categories





# b. White meat (per 100g/day)

Begg's funnel plot with pseudo 95% confidence limits



Figure S6. Begg's funnel plot of studies for white meat consumption and gastric cancer risk. (a) Funnel plot of the highest versus lowest categories of white meat consumption and gastric cancer risk.; (b) Funnel plot of 100g/day increase in white meat consumption and gastric cancer risk.