Kunutsor, S. K., Whitehouse, M. R., Blom, A. W., & Laukkanen, J. A. (2017). Low serum magnesium levels are associated with increased risk of fractures: a long-term prospective cohort study. European Journal of Epidemiology, 32(7), 593-603. https://doi.org/10.1007/s10654-017-0242-2
APPENDIX SUPPLEMENTS

Low serum magnesium levels are associated with increased risk of fractures: A long-term prospective cohort study

| Appendix 1 | STROBE 2007 Statement—Checklist of items that should be included in reports of cohort studies |
| Appendix 2 | Baseline participant characteristics by quartiles of serum magnesium |
| Appendix 3 | Hazard ratios for incident femoral fractures by quartiles of serum magnesium levels |
| Appendix 4 | Association of serum magnesium and incident fractures by quartiles of serum magnesium (with quartile 1 as a reference comparison) |
## Appendix 1: STROBE 2007 Statement

| Section/Topic          | Item # | Recommendation                                                                 | Reported on page # |
|------------------------|--------|-------------------------------------------------------------------------------|--------------------|
| Title and abstract     | 1      | (a) Indicate the study’s design with a commonly used term in the title or the abstract | Page 1             |
|                        |        | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 2             |
| Introduction           |        |                                                                               |                    |
| Background/rationale   | 2      | Explain the scientific background and rationale for the investigation being reported | Page 3-4          |
| Objectives             | 3      | State specific objectives, including any prespecified hypotheses               | Page 3-4          |
| Methods                |        |                                                                               |                    |
| Study design           | 4      | Present key elements of study design early in the paper                        | Study Design and Participants |
| Setting                | 5      | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Study Design and Participants |
| Participants           | 6      | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Study Design and Participants |
|                        |        | (b) For matched studies, give matching criteria and number of exposed and unexposed | Not applicable     |
| Variables              | 7      | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Risk Factor Assessment |
| Data sources/measurement| 8*    | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | Risk Factor Assessment |
| Bias                   | 9      | Describe any efforts to address potential sources of bias                       | Statistical Analyses |
| Study size             | 10     | Explain how the study size was arrived at                                       | Statistical Analyses |
| Quantitative variables | 11     | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Statistical Analyses |
| Statistical methods    | 12     | (a) Describe all statistical methods, including those used to control for confounding | Statistical Analyses |
|                        |        | (b) Describe any methods used to examine subgroups and interactions             | Statistical Analyses |
|                        |        | (c) Explain how missing data were addressed                                     | Not applicable     |
|                        |        | (d) If applicable, explain how loss to follow-up was addressed                  | Not applicable     |
| Results | Statistical Analyses |
|---------------------|----------------------|
| **Participants** 13* | Study population |
| (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed |
| (b) Give reasons for non-participation at each stage |
| (c) Consider use of a flow diagram |
| **Descriptive data** 14* | Results; Table 1; Appendix 2 |
| (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders |
| (b) Indicate number of participants with missing data for each variable of interest |
| (c) Summarise follow-up time (eg, average and total amount) |
| **Outcome data** 15* | Results |
| Report numbers of outcome events or summary measures over time |
| **Main results** 16 | Results; Tables 2-4 |
| (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| (b) Report category boundaries when continuous variables were categorized |
| (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| **Other analyses** 17 | Results; Figure 2 |
| Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | Discussion - Summary of main findings |
| **Key results** 18 | |
| Summarise key results with reference to study objectives |
| **Limitations** | Discussion |
| Interpretation 20 | |
| Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| **Generalisability** 21 | Discussion |
| Discuss the generalisability (external validity) of the study results |
| **Other information** | |
| Funding 22 | Page 16 |
| Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |
Appendix 2. Baseline participant characteristics by quartiles of serum magnesium

| Magnesium (mg/dl) | Quartile 1 Mean (SD), or n (%) | Quartile 2 Mean (SD), or n (%) | Quartile 3 Mean (SD), or n (%) | Quartile 4 Mean (SD), or n (%) | P-value |
|------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|---------|
|                  | Mean (SD), median (IQR), or n (%) | Mean (SD), median (IQR), or n (%) | Mean (SD), median (IQR), or n (%) | Mean (SD), median (IQR), or n (%) |         |
|                  | 1.79 (0.09)                  | 1.93 (0.03)                  | 2.03 (0.3)                  | 2.17 (0.08)                  | < 0.0001|

**Questionnaire/Prevalent conditions**

| Age at survey (years) | 53.1 (5.5)   | 52.4 (5.7)   | 53.3 (4.8)   | 53.7 (3.9)   | 0.0002  |
| Alcohol consumption (g/week) | 86.8 (170.8) | 78.9 (154.8) | 71.6 (101.1) | 66.0 (110.3) | 0.063   |
| Total energy intake, kJ/day | 9,998 (2,736) | 9,900 (2,676) | 9,871 (2,557) | 9,647 (2,450) | 0.143   |
| Socioeconomic status | 8.70 (4.09)   | 8.46 (4.24)   | 8.60 (4.30)   | 8.26 (4.33)   | 0.339   |

**Dietary magnesium intake (mg/day)**

| History of diabetes | No | Yes | No | Yes | P-value |
|---------------------|----|-----|----|-----|---------|
| No                  | 527 (93.1) | 534 (95.7) | 551 (97.7) | 544 (97.7) |         |
| Yes                 | 39 (6.9)  | 24 (4.3)  | 13 (2.3)  | 13 (2.3)  | < 0.001 |

**Smoking status**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| No                      | 387 (68.4) | 387 (69.4) | 394 (69.9) | 396 (71.1) | 0.796   |
| Yes                     | 179 (31.6) | 171 (30.7) | 170 (30.1) | 161 (28.9) |         |

**Physical measurements**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| BMI (kg/m²) | 27.2 (3.8) | 26.7 (3.5) | 27.0 (3.5) | 26.9 (3.5) | 0.209   |
| Height (cm) | 173.0 (6.1) | 172.9 (6.3) | 172.9 (6.3) | 172.5 (6.2) | 0.560   |
| DBP (mmHg) | 89 (11)  | 88 (10)   | 89 (10)   | 88 (11)   | 0.513   |

**Physical activity (kJ/day)**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| 1,500 (1,414) | 1,596 (1,658) | 1,547 (1,370) | 1,540 (1,502) | 0.760   |

**Lipid markers**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| Total cholesterol (mmol/l) | 5.82 (1.13) | 5.82 (1.10) | 5.93 (1.02) | 6.06 (1.05) | 0.0002  |
| HDL-C (mmol/l) | 1.31 (0.33) | 1.29 (0.29) | 1.29 (0.28) | 1.28 (0.29) | 0.485   |
| Triglycerides (mmol/l) | 1.08 (0.79-1.53) | 1.08 (0.79-1.52) | 1.11 (0.80-1.57) | 1.12 (0.83-1.64) | 0.118   |

**Metabolic and renal markers**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| Fasting plasma glucose (mmol/l) | 5.73 (1.96) | 5.25 (0.96) | 5.24 (0.79) | 5.22 (0.94) | < 0.0001|
| Serum creatinine (µmol/l) | 87.2 (15.3) | 89.1 (14.3) | 89.9 (12.5) | 92.7 (34.8) | 0.0002  |
| Estimated GFR (ml/min/1.73 m²) | 90.1 (17.7) | 87.7 (15.7) | 86.1 (19.0) | 84.0 (15.7) | < 0.0001|

**Trace elements**

| History of hypertension | No | Yes | No | Yes | P-value |
|-------------------------|----|-----|----|-----|---------|
| Serum zinc (mg/l) | 0.92 (0.13) | 0.94 (0.12) | 0.94 (0.11) | 0.95 (0.12) | 0.0006  |
| Serum ionized calcium (mmol/l) | 1.18 (0.05) | 1.18 (0.05) | 1.18 (0.05) | 1.18 (0.05) | 0.016   |
| Serum potassium (mmol/l) | 3.93 (0.28) | 3.93 (0.37) | 3.92 (0.27) | 3.90 (0.29) | 0.171   |

BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; SD, standard deviation; SBP, systolic blood pressure;
Appendix 3. Hazard ratios for incident femoral fractures by quartiles of serum magnesium levels

A, adjusted for age; B, adjusted for age, body mass index, height, systolic blood pressure, smoking status, history of diabetes, alcohol consumption, and physical activity; the mean magnesium level (mg/dl) was 1.79 for the lowest quartile; 1.93 for the second quartile; 2.03 for the third quartile; and 2.17 for the top quartile; CI, confidence interval
### Appendix 4. Association of serum magnesium and incident fractures by quartiles of serum magnesium (with quartile 1 as reference comparison)

| Serum magnesium (mg/dl) | Events/Total | Model 1 | Model 2 | Model 3 |
|-------------------------|--------------|---------|---------|---------|
|                         |              | HR (95% CI) | P-value | HR (95% CI) | P-value | HR (95% CI) | P-value |
| **Total fractures**     |              |         |         |         |         |
| Q1 (0.92-1.88)          | 46 / 566     | ref     | ref     | ref     |
| Q2 (1.88-1.98)          | 27 / 558     | 0.53 (0.33 to 0.86) | 0.010 | 0.55 (0.34 to 0.89) | 0.015 | 0.56 (0.35 to 0.91) | 0.019 |
| Q3 (1.98-2.08)          | 24 / 564     | 0.44 (0.27 to 0.72) | 0.001 | 0.46 (0.28 to 0.76) | 0.002 | 0.48 (0.29 to 0.79) | 0.004 |
| Q4 (2.08-2.55)          | 26 / 557     | 0.48 (0.29 to 0.77) | 0.003 | 0.50 (0.31 to 0.82) | 0.005 | 0.56 (0.34 to 0.91) | 0.019 |
| **Femoral fractures**   |              |         |         |         |         |
| Q1 (0.92-1.88)          | 31 / 559     | ref     | ref     | ref     |
| Q2 (1.88-1.98)          | 16 / 553     | 0.47 (0.26 to 0.86) | 0.014 | 0.49 (0.27 to 0.90) | 0.022 | 0.51 (0.27 to 0.94) | 0.031 |
| Q3 (1.98-2.08)          | 16 / 556     | 0.42 (0.23 to 0.77) | 0.005 | 0.44 (0.24 to 0.81) | 0.009 | 0.47 (0.26 to 0.87) | 0.017 |
| Q4 (2.08-2.55)          | 15 / 556     | 0.39 (0.21 to 0.73) | 0.003 | 0.41 (0.22 to 0.77) | 0.005 | 0.47 (0.25 to 0.88) | 0.019 |

CI, confidence interval; HR, hazard ratio; ref, reference; Q, quartile

Model 1: Adjusted for age

Model 2: Model 1 plus body mass index, height, systolic blood pressure, smoking, history of diabetes, alcohol consumption, and physical activity

Model 3: Model 2 plus estimated glomerular filtration rate, socioeconomic status, total energy intake, serum zinc, serum potassium, and serum ionized calcium