

## ORIGINAL ARTICLE

# Mendelian Randomization Analyses Explore the Relationship between Trace Elements and Prostate Cancer

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### SUMMARY

**Background:** Trace elements indeed play a significant role in the occurrence and development of cancers, but it remains ambiguous whether a causal relationship exists between trace elements and prostate cancer. This study employed Mendelian randomization analyses to investigate such a causal link between trace elements (Co, Fe, Mg, Se, and Zn) and prostate cancer.

**Methods:** The analyses primarily utilized the inverse variance weighted (IVW) method, supplemented by MR-Egger, weighted median, simple mode, and MR-PRESSO.

**Results:** The results of IVW (OR = 1.005, 95% CI: 1.001 - 1.009,  $p = 0.014$ ) and MR-PRESSO (OR = 1.005, 95% CI: 1.002 - 1.008,  $p = 0.015$ ) analyses demonstrated a significant causal effect of Mg on genetically predicted prostate cancer. However, the IVW analysis did not reveal any causal associations between prostate cancer and Co, Fe, Se, or Zn.

**Conclusions:** Our study provided compelling evidence of a causal relationship between magnesium and prostate cancer within the European population. Therefore, maintaining magnesium balance may emerge as a potent strategy for prostate cancer prevention.

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## Supplementary Data

Table S1. Mendelian randomization analysis of the levels of five common mineral elements and the occurrence of prostate cancer.

| MR info   |      |                 |           |        |                             |        | Cochran's Q |      |        | Horizontal pleiotropy |        |        |
|-----------|------|-----------------|-----------|--------|-----------------------------|--------|-------------|------|--------|-----------------------|--------|--------|
| Exposures | nSNP | Method          | $\beta$   | SE     | OR [95% CI]                 | p      | Q           | Q_df | p      | Intercept             | SE     | p      |
| Calcium   | 16   | MR Egger        | 0.0128    | 0.0157 | 1.0129<br>[0.9821 - 1.0446] | 0.4296 | 16.5521     | 14   | 0.2808 | -0.0004               | 0.0005 | 0.4324 |
|           |      | IVW             | 0.0002    | 0.0018 | 1.0002<br>[0.9966 - 1.0037] | 0.9270 | 17.3246     | 15   | 0.2998 | -                     | -      | -      |
|           |      | Weighted median | 0.0024    | 0.0023 | 1.0024<br>[0.9978 - 1.007]  | 0.3008 | -           | -    | -      | -                     | -      | -      |
|           |      | Simple mode     | 0.0037    | 0.0046 | 1.0037<br>[0.9948 - 1.0128] | 0.4279 | -           | -    | -      | -                     | -      | -      |
|           |      | MR-PRESSO       | 0.0002    | 0.0018 | 1.0002<br>[0.9966 - 1.0037] | 0.9282 | -           | -    | -      | -                     | -      | -      |
| Iron      | 11   | MR Egger        | 0.0245    | 0.0212 | 1.0248<br>[0.9831 - 1.0683] | 0.2777 | 14.6160     | 9    | 0.1020 | -0.0007               | 0.0006 | 0.2650 |
|           |      | IVW             | -0.0005   | 0.0027 | 0.9995<br>[0.9943 - 1.0047] | 0.8474 | 16.9104     | 10   | 0.0763 | -                     | -      | -      |
|           |      | Weighted median | 0.0029    | 0.0028 | 1.0029<br>[0.9975 - 1.0083] | 0.2897 | -           | -    | -      | -                     | -      | -      |
|           |      | Simple mode     | 0.0037    | 0.0035 | 1.0037<br>[0.9969 - 1.0105] | 0.3092 | -           | -    | -      | -                     | -      | -      |
|           |      | MR-PRESSO       | -0.0005   | 0.0027 | 0.9995<br>[0.9943 - 1.0047] | 0.8513 | -           | -    | -      | -                     | -      | -      |
| Magnesium | 13   | MR Egger        | -0.0096   | 0.0228 | 0.9904<br>[0.9471 - 1.0357] | 0.6810 | 8.6207      | 11   | 0.6569 | 0.0004                | 0.0006 | 0.5404 |
|           |      | IVW             | 0.0047    | 0.0019 | 1.0047<br>[1.0010 - 1.0085] | 0.0136 | 9.0200      | 12   | 0.7012 | -                     | -      | -      |
|           |      | Weighted median | 0.0043    | 0.0025 | 1.0043<br>[0.9993 - 1.0093] | 0.0938 | -           | -    | -      | -                     | -      | -      |
|           |      | Simple mode     | 0.0046    | 0.0042 | 1.0046<br>[0.9963 - 1.0130] | 0.3006 | -           | -    | -      | -                     | -      | -      |
|           |      | MR-PRESSO       | 0.0047    | 0.0017 | 1.0047<br>[1.0015 - 1.0080] | 0.0147 | -           | -    | -      | -                     | -      | -      |
| Selenium  | 8    | MR Egger        | 5.28e-06  | 0.0015 | 1.0000<br>[0.9971 - 1.0029] | 0.9973 | 3.5649      | 6    | 0.7353 | 8.92e-05              | 0.0002 | 0.7126 |
|           |      | IVW             | 0.0006    | 0.0004 | 1.0006<br>[0.9997 - 1.0014] | 0.2049 | 3.7141      | 7    | 0.8121 | -                     | -      | -      |
|           |      | Weighted median | 0.0002    | 0.0006 | 1.0002<br>[0.9991 - 1.0014] | 0.6983 | -           | -    | -      | -                     | -      | -      |
|           |      | Simple mode     | -9.76e-05 | 0.0009 | 0.9999<br>[0.9982 - 1.0016] | 0.9147 | -           | -    | -      | -                     | -      | -      |
|           |      | MR-PRESSO       | 0.0002    | 0.0004 | 1.0002<br>[0.9994 - 1.0010] | 0.6006 | -           | -    | -      | -                     | -      | -      |
| Zinc      | 5    | MR Egger        | 0.0003    | 0.0017 | 1.0003<br>[0.997 - 1.0036]  | 0.8616 | 31.8313     | 3    | 0.8639 | -0.0002               | 0.0003 | 0.6531 |
|           |      | IVW             | -0.0005   | 0.0005 | 0.9995<br>[0.9986 - 1.0005] | 0.3114 | 32.5952     | 4    | 0.9118 | -                     | -      | -      |
|           |      | Weighted median | -0.0004   | 0.0006 | 0.9996<br>[0.9985 - 1.0008] | 0.5444 | -           | -    | -      | -                     | -      | -      |
|           |      | Simple mode     | -0.0004   | 0.0007 | 0.9996<br>[0.9982 - 1.0011] | 0.6456 | -           | -    | -      | -                     | -      | -      |
|           |      | MR-PRESSO       | -0.0005   | 0.0002 | 0.9995<br>[0.9991 - 0.9999] | 0.0762 | -           | -    | -      | -                     | -      | -      |