|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sensitivity analysis | Iodine  level | Iodine2  (µg/L) |  | All |  |  | Low selenium2 (≤92.0 µg/L) | | |  | High selenium2 (≥88.0 µg/L) | | |
|  |  |  | Cases/  Controls | OR (95 CI) | OR1 (95 CI) |  | Cases/  Controls | OR (95 CI) | OR2 (95 CI) |  | Cases/  Controls | OR (95 CI) | OR2 (95 CI) |
| Main analysis | Low | ≤70.9 | 525/490 | 1 | 1 |  | 290/288 | 1 | 1 |  | 235/202 | 1 | 1 |
|  | High | ≥65.6 | 504/514 | 0.92  (0.77-1.09) | 0.92  (0.76-1.10) |  | 230/206 | 1.11  (0.87-1.42) | 1.15  (0.87-1.50) |  | 274/308 | **0.76**  **(0.60-0.98)** | **0.75**  **(0.57-0.99)** |
| Excluding cases within 2 years | Low | ≤70.9 | 489/490 | 1 | 1 |  | 265/288 | 1 | 1 |  | 224/202 | 1 | 1 |
| from baseline | High | ≥65.6 | 458/514 | 0.89  (0.75-1.07) | 0.90  (0.74-1.08) |  | 207/206 | 1.09  (0.85-1.41) | 1.15  (0.87-1.52) |  | 251/308 | **0.74**  **(0.57-0.95)** | **0.72**  **(0.55-0.96)** |
| Excluding *in situ* cases | Low | ≤70.9 | 485/490 | 1 | 1 |  | 266/288 | 1 | 1 |  | 219/202 | 1 | 1 |
|  | High | ≥65.6 | 451/514 | 0.89  (0.74-1.06) | 0.88  (0.73-1.07) |  | 205/206 | 1.08  (0.83-1.39) | 1.12  (0.85-1.48) |  | 246/308 | **0.74**  **(0.57-0.95)** | **0.72**  **(0.54-0.95)** |
| ER-positive  cases | Low | ≤70.9 | 385/490 | 1 | 1 |  | 207/288 | 1 | 1 |  | 178/202 | 1 | 1 |
|  | High | ≥65.6 | 341/514 | 0.84  (0.70-1.02) | 0.84  (0.67-1.03) |  | 159/206 | 1.07  (0.82-1.41) | 1.09  (0.81-1.46) |  | 182/308 | **0.67**  **(0.51-0.88)** | **0.66**  **(0.49-0.89)** |
| ER-negative cases | Low | ≤70.9 | 42/490 | 1 | 1 |  | 26/288 | 1 | 1 |  | 16/202 | 1 | 1 |
|  | High | ≥65.6 | 43/514 | 0.98  (0.63-1.52) | 1.02  (0.63-1.63) |  | 15/206 | 0.81  (0.42-1.56) | 0.90  (0.42-1.92) |  | 28/308 | 1.15  (0.61-2.18) | 1.05  (0.51-2.17) |
| Adjusted for dietary factors3 | Low | ≤70.9 | 525/490 | 1 | 1 |  | 290/288 | 1 | 1 |  | 235/202 | 1 | 1 |
|  | High | ≥65.6 | 504/514 | 0.92  (0.77-1.09) | 0.92  (0.76-1.10) |  | 230/206 | 1.14  (0.89-1.47) | 1.17  (0.89-1.55) |  | 274/308 | **0.75**  **(0.59-0.97)** | **0.74**  **(0.56-0.98)** |

Supplementary table 1. Iodine levels and breast cancer risk, overall and stratified for selenium levels. In relation to estrogen receptor (ER) status, and following additional

exclusions and adjustments.

1,2 Same adjustments as in main analysis, table 2.

3Vitamin D, calcium, beta-carotene, and total energy intake in addition to other factors.

Supplementary table 2. Iodine levels and breast cancer risk, overall and stratified for selenium levels with regard to menopausal status, age at diagnosis and follow-up.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sensitivity analysis | Iodine  level | Iodine2  (µg/L) | All | | |  | Low selenium2 (≤92.0 µg/L) | | |  | High selenium2 (≥88.0 µg/L) | | |
|  |  |  | Cases/  Controls | OR (95 CI) | OR1 (95 CI) |  | Cases/  Controls | OR (95 CI) | OR2 (95 CI) |  | Cases/  Controls | OR (95 CI) | OR2 (95 CI) |
| Pre/peri-menopausal | Low | ≤70.9 | 238/177 | 1 | 1 |  | 138/103 | 1 | 1 |  | 100/74 | 1 | 1 |
|  | High | ≥65.6 | 179/142 | 0.94  (0.70-1.26) | 0.88  (0.64-1.21) |  | 91/75 | 0.91  (0.61-1.35) | 0.95  (0.60-1.49) |  | 88/67 | 0.97  (0.63-1.51) | 0.94  (0.57-1.55) |
| Post-  menopausal | Low | ≤70.9 | 287/313 | 1 | 1 |  | 152/185 | 1 | 1 |  | 135/128 | 1 | 1 |
|  | High | ≥65.6 | 325/372 | 0.95  (0.77-1.19) | 0.93  (0.74-1.17) |  | 139/131 | 1.29  (0.94-1.78) | 1.36  (0.94-1.96) |  | 186/241 | **0.73**  **(0.54-0.996)** | **0.68**  **(0.48-0.96)** |
| Age at diagnosis  <55 years | Low | ≤70.9 | 54/490 | 1 | 1 |  | 37/288 | 1 | 1 |  | 17/202 | 1 | 1 |
|  | High | ≥65.6 | 47/514 | 0.83  (0.55-1.25) | 0.92  (0.57-1.51) |  | 23/206 | 0.87  (0.50-1.51) | 0.76  (0.37-1.56) |  | 24/308 | 0.93  (0.49-1.77) | 1.24  (0.48-3.18) |
| Age at diagnosis  ≥55-65 years | Low | ≤70.9 | 186/490 | 1 | 1 |  | 96/288 | 1 | 1 |  | 90/202 | 1 | 1 |
|  | High | ≥65.6 | 182/514 | 0.93  (0.73-1.18) | 1.04  (0.79-1.36) |  | 89/206 | 1.30  (0.92-1.82) | 1.30  (0.88-1.92) |  | 93/308 | **0.68**  **(0.48-0.95)** | 0.81  (0.52-1.26) |
| Age at diagnosis  ≥65 years | Low | ≤70.9 | 285/490 | 1 | 1 |  | 157/288 | 1 | 1 |  | 128/202 | 1 | 1 |
|  | High | ≥65.6 | 275/514 | 0.92  (0.75-1.13) | 0.83  (0.66-1.04) |  | 118/206 | 1.05  (0.78-1.42) | 0.97  (0.68-1.37) |  | 157/308 | 0.80  (0.60-1.08) | **0.71**  **(0.51-0.99)** |
| Short follow-up  (below median, | Low | ≤70.9 | 216/490 | 1 | 1 |  | 111/288 | 1 | 1 |  | 105/202 | 1 | 1 |
| <10.22 years) | High | ≥65.6 | 275/514 | 1.21  (0.98-1.51) | 1.18  (0.94-1.48) |  | 125/206 | **1.57**  **(1.15-2.15)** | **1.57**  **(1.12-2.21)** |  | 150/308 | 0.94  (0.69-1.27) | 0.88  (0.62-1.25) |
| Long follow-up  (above median, | Low | ≤70.9 | 309/490 | 1 | 1 |  | 179/288 | 1 | 1 |  | 130/202 | 1 | 1 |
| ≥10.22 years) | High | ≥65.6 | 229/514 | **0.71**  **(0.57-0.87)** | **0.72**  **(0.57-0.90)** |  | 105/206 | 0.82  (0.61-1.11) | 0.86  (0.62-1.20) |  | 124/308 | **0.63**  **(0.46-0.85)** | **0.59**  **(0.42-0.84)** |

1,2 Same adjustments as in main analysis, table 2.