**Supplementary Table 1.** Multivariate association between potential determinants and TPOAb detectability, positivity, and persistent TPOAb positivity in two and three visits, according to sex.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **OR (95%CI)** | | | | | | | |
|  | **TPOAb detectability** | | **TPOAb positivity** | | **TPOAb positivity in two visits** | | **TPOAb positivity in three visits** | |
|  | **Male (n=6003)** | **Female (n=7184)** | **Male (n=6003)** | **Female (n=7184)** | **Male (n=5561)** | **Female (n=6709)** | **Male (n=4610)** | **Female (n=5814)** |
| **Age,** per 10 years | 0.91 (0.80-1.04) | 0.90 (0.78-1.03) | 1.03 (0.93-1.15) | 1.02 (0.94-1.10) | 0.96 (0.85-1.08) | 0.94 (0.87-1.03) | 1.02 (0.88-1.18) | 0.94 (0.85-1.03) |
| **BMI,** kg/m² | **1.04 (1.01-1.07)** | 1.02 (0.99-1.05) | 1.01 (0.99-1.03) | 1.01 (0.99-1.02) | 1.02 (0.99-1.04) | 1.00 (0.99-1.02) | 1.01 (0.98-1.04) | 1.00 (0.98-1.02) |
| **Self-reported race** |  |  |  |  |  |  |  |  |
| White | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Mixed | **0.39 (0.30-0.52)** | **0.34 (0.26-0.45)** | 0.85 (0.68-1.08) | 0.87 (0.74-1.02) | 0.92 (0.72-1.18) | 0.92 (0.78-1.10) | 0.81 (0.60-1.11) | 0.95 (0.77-1.17) |
| Black | **0.35 (0.25-0.50)** | **0.34 (0.24-0.47)** | 0.92 (0.68-1.26) | **0.73 (0.60-0.90)** | 0.86 (0.61-1.21) | 0.81 (0.65-1.00) | 0.76 (0.50-1.16) | 0.88 (0.68-1.13) |
| Others | 1.10 (0.48-2.55) | 0.86 (0.41-1.80) | 1.03 (0.62-1.70) | **0.54 (0.36-0.81)** | 1.08 (0.62-1.87) | **0.56 (0.36-0.87)** | 0.99 (0.50-1.93) | 0.67 (0.41-1.09) |
| **Education** |  |  |  |  |  |  |  |  |
| Lower | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Intermediate | **0.65 (0.43-0.98)** | **0.54 (0.31-0.95)** | 1.10 (0.81-1.48) | 1.02 (0.80-1.31) | 1.10 (0.79-1.53) | 1.09 (0.83-1.44) | 0.97 (0.65-1.45) | 1.33 (0.93-1.89) |
| Higher | **0.42 (0.28-0.62)** | **0.32 (0.18-0.56)** | 1.15 (0.86-1.54) | 0.93 (0.72-1.19) | 1.10 (0.80-1.52) | 0.94 (0.71-1.25) | 0.89 (0.60-1.32) | 1.10 (0.77-1.57) |
| **Alcohol intake** |  |  |  |  |  |  |  |  |
| None | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| No heavy drinking | 0.96 (0.75-1.24) | 1.05 (0.81-1.37) | 0.99 (0.81-1.22) | 0.92 (0.79-1.07) | 1.08 (0.86-1.35) | 0.97 (0.83-1.13) | 1.01 (0.77-1.33) | 0.95 (0.79-1.15) |
| Heavy drinking | 0.82 (0.56-1.21) | **0.54 (0.30-0.96)** | 0.88 (0.63-1.23) | 0.82 (0.55-1.21) | 0.99 (0.69-1.42) | 0.94 (0.63-1.41) | 0.94 (0.60-1.47) | 1.03 (0.65-1.64) |
| **Smoking status** |  |  |  |  |  |  |  |  |
| Never | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Former | 1.27 (0.98-1.65) | 1.22 (0.92-1.61) | 1.10 (0.89-1.36) | 1.10 (0.94-1.29) | 1.19 (0.95-1.51) | **1.19 (1.01-1.40)** | 1.03 (0.77-1.37) | 1.10 (0.91-1.34) |
| Current | **2.71 (1.69-4.34)** | **5.47 (2.66-11.24)** | 0.89 (0.65-1.23) | 1.06 (0.85-1.31) | 1.03 (0.73-1.45) | 1.13 (0.89-1.42) | 1.18 (0.79-1.76) | 1.26 (0.96-1.65) |
| **Parity** |  |  |  |  |  |  |  |  |
| No | - | Ref. | - | Ref. | - | Ref. | - | Ref. |
| Yes | - | 0.84 (0.64-1.12) | - | 0.93 (0.79-1.08) | - | 0.97 (0.82-1.15) | - | 0.93 (0.77-1.14) |

Legend: OR: odds ratio. 95%CI: 95% confidence interval. Statistically significant results are in bold.

Multivariate model adjusted for age, BMI, race, education, smoking status, alcohol intake, rheumatic diseases, parity (only women), FT4 and TSH.

**Supplementary Table 2.** Multivariate association between determinants and thyroid peroxidase antibody categories according to sex (male: n=6003; female: n=7184).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TPOAb categories** | | | |
|  | Undetectable  (≤ 5.00 IU/ml) | Low detectable (5.01-14.99 IU/ml) | High detectable (15.00-33.99 IU/ml) | Positive  (≥ 34.00 IU/ml) |
| **Age,** per 10 years |  |  |  |  |
| Male | Ref. | 0.90 (0.79-1.03) | 0.94 (0.81-1.08) | 0.94 (0.80-1.11) |
| Female | Ref. | 0.90 (0.78-1.03) | 0.88 (0.76-1.03) | 0.92 (0.79-1.07) |
| **BMI,** kg/m² |  |  |  |  |
| Male | Ref. | **1.04 (1.01-1.07)** | **1.03 (1.00-1.07)** | **1.04 (1.01-1.08)** |
| Female | Ref. | 1.02 (0.99-1.05) | 1.02 (0.99-1.05) | **1.03 (1.00-1.06)** |
| **Race, other vs. White** |  |  |  |  |
| Male | Ref. | 1.11 (0.48-2.57) | 1.07 (0.46-2.61) | 1.13 (0.44-2.94) |
| Female | Ref. | 0.91 (0.43-1.91) | 0.99 (0.46-2.16) | 0.50 (0.22-1.13) |
| **Race, Black vs. White** |  |  |  |  |
| Male | Ref. | **0.36 (0.26-0.51)** | **0.31 (0.21-0.45)** | **0.34 (0.22-0.54)** |
| Female | Ref. | **0.35 (0.25-0.49)** | **0.31 (0.22-0.45)** | **0.26 (0.18-0.38)** |
| **Race, Mixed vs. White** |  |  |  |  |
| Male | Ref. | **0.40 (0.30-0.53)** | **0.37 (0.28-0.51)** | **0.35 (0.25-0.50)** |
| Female | Ref. | **0.35 (0.27-0.47)** | **0.31 (0.23-0.42)** | **0.31 (0.23-0.43)** |
| **Education, higher vs. lower** | | |  |  |
| Male | Ref. | **0.44 (0.29-0.66)** | **0.32 (0.21-0.49)** | **0.49 (0.30-0.80)** |
| Female | Ref. | **0.34 (0.19-0.59)** | **0.27 (0.15-0.49)** | **0.31 (0.17-0.57)** |
| **Education, intermediate vs. lower** | | |  |  |
| Male | Ref. | 0.67 (0.45-1.02) | **0.56 (0.36-0.86)** | 0.72 (0.44-1.18) |
| Female | Ref. | **0.54 (0.30-0.95)** | **0.53 (0.29-0.95)** | 0.56 (0.31-1.02) |
| **Alcohol intake, heavy drinking vs. none** | |  |  |  |
| Male | Ref. | 0.85 (0.57-1.25) | 0.78 (0.51-1.19) | 0.74 (0.45-1.21) |
| Female | Ref. | 0.57 (0.32-1.02) | **0.48 (0.25-0.92)** | **0.46 (0.23-0.90)** |
| **Alcohol intake, no heavy drinking vs. none** | | |  |  |
| Male | Ref. | 0.97 (0.75-1.24) | 0.95 (0.72-1.26) | 0.96 (0.70-1.31) |
| Female | Ref. | 1.04 (0.80-1.36) | 1.12 (0.84-1.50) | 0.97 (0.73-1.30) |
| **Smoking status, current vs. never** | |  |  |  |
| Male | Ref. | **2.22 (1.38-3.57)** | **5.05 (3.09-8.26)** | **2.36 (1.35-4.13)** |
| Female | Ref. | **4.42 (2.14-9.10)** | **9.50 (4.57-19.77)** | **5.51 (2.61-11.60)** |
| **Smoking status, former vs. never** | |  |  |  |
| Male | Ref. | 1.25 (0.96-1.63) | 1.34 (0.99-1.79) | 1.37 (0.98-1.90) |
| Female | Ref. | 1.19 (0.90-1.58) | 1.26 (0.92-1.71) | 1.31 (0.96-1.79) |
| **Parity, yes vs. no** |  |  |  |  |
| Female | Ref. | 0.84 (0.64-1.11) | 0.89 (0.66-1.21) | 0.80 (0.58-1.08) |

Legend: OR: odds ratio. 95%CI: 95% confidence interval. Statistically significant results are in bold.

Multivariate model adjusted for age, BMI, race, education, smoking status, alcohol intake, rheumatic disease, parity (only women), TSH, and FT4.

**Supplementary Table 3.** Sensitivity analyses of the association between potential determinants and TPOAb detectability and positivity.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **TPOAb detectability OR (95%CI)** | | | **TPOAb positivity OR (95%CI)** | | |
|  | **Sensitivity analysis 1** | **Sensitivity analysis 2** | **Sensitivity analysis 3** | **Sensitivity analysis 1** | **Sensitivity analysis 2** | **Sensitivity analysis 3** |
| **Age,** per 10 years | **0.91 (0.83-0.99)** | 0.91 (0.82-1.01) | 0.93 (0.84-1.03) | 1.03 (0.96-1.11) | 1.02 (0.95-1.10) | **1.12 (1.02-1.21)** |
| **BMI,** kg/m² | **1.03 (1.01-1.05)** | **1.03 (1.01-1.05)** | **1.03 (1.00-1.05)** | 1.00 (0.99-1.02) | 1.01 (0.99-1.02) | 1.00 (0.99-1.02) |
| **Sex** |  |  |  |  |  |  |
| Male | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Female | **1.35 (1.13-1.62)** | **1.32 (1.09-1.59)** | **1.30 (1.07-1.57)** | **1.70 (1.48-1.95)** | **1.78 (1.54-2.05)** | **1.73 (1.47-2.03)** |
| **Race** |  |  |  |  |  |  |
| White | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Mixed | **0.38 (0.31-0.46)** | **0.39 (0.32-0.48)** | **0.41 (0.33-0.51)** | 0.89 (0.77-1.04) | 0.87 (0.74-1.02) | 0.94 (0.79-1.13) |
| Black | **0.37 (0.29-0.47)** | **0.38 (0.29-0.49)** | **0.39 (0.30-0.51)** | 0.93 (0.77-1.12) | 0.94 (0.77-1.14) | 0.95 (0.76-1.18) |
| Others | 0.97 (0.56-1.68) | 1.07 (0.59-1.93) | 1.02 (0.56-1.85) | 0.75 (0.52-1.08) | 0.73 (0.50-1.08) | 0.74 (0.48-1.15) |
| **Education** |  |  |  |  |  |  |
| Lower | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Intermediate | **0.60 (0.43-0.84)** | **0.60 (0.42-0.85)** | **0.60 (0.42-0.87)** | 0.96 (0.78-1.19) | 0.99 (0.80-1.24) | 0.97 (0.75-1.24) |
| Higher | **0.38 (0.27-0.52)** | **0.38 (0.27-0.54)** | **0.37 (0.26-0.53)** | 0.92 (0.75-1.13) | 0.94 (0.76-1.17) | 0.91 (0.71-1.17) |
| **Alcohol intake** |  |  |  |  |  |  |
| None | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| No heavy drinking | 1.01 (0.84-1.22) | 0.97 (0.80-1.17) | 0.96 (0.79-1.17) | 0.94 (0.82-1.08) | 0.94 (0.82-1.09) | 0.98 (0.83-1.15) |
| Heavy drinking | 0.74 (0.54-1.03) | **0.69 (0.50-0.96)** | **0.70 (0.50-0.98)** | 0.90 (0.68-1.18) | 0.90 (0.68-1.19) | 0.78 (0.56-1.09) |
| **Smoking status** |  |  |  |  |  |  |
| Never | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Former | **1.24 (1.01-1.51)** | 1.22 (0.99-1.49) | 1.21 (0.98-1.49) | 1.08 (0.93-1.24) | 1.05 (0.91-1.23) | 0.96 (0.81-1.15) |
| Current | **3.47 (2.33-5.15)** | **3.54 (2.35-5.35)** | **3.36 (2.22-5.08)** | 1.02 (0.83-1.24) | 1.05 (0.85-1.29) | 0.96 (0.76-1.22) |

Legend: BMI: Body mass index. OR: odds ratio. 95%CI: 95% confidence interval. Statistically significant results are in bold.

Model adjusted for age, sex, BMI, race, education, smoking status, alcohol intake, rheumatic diseases, FT4, and TSH.

**Sensitivity analysis 1 -** Excluding participants using medication to treat thyroid diseases. **Sensitivity analysis 2 -** Plus excluding for the use of medications that interfere on thyroid function. **Sensitivity analysis 3 -** Plus excluding participants with abnormal thyroid function.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Persistent TPOAb positivity in two visits** | | | **Persistent TPOAb positivity in three visits** | | |
|  | **Sensitivity analysis 1**  (n=1026/11391) | **Sensitivity analysis 2**  (n=962/10619) | **Sensitivity analysis 3**  (n=690/9440) | **Sensitivity analysis 1**  (n=670/9672) | **Sensitivity analysis 2**  (n=653/9041) | **Sensitivity analysis 3**  (n=452/8031) |
| **Age,** per 10 years | 0.93 (0.86-1.01) | 0.94 (0.87-1.02) | 1.01 (0.92-1.11) | 0.97 (0.88-1.07) | 0.96 (0.87-1.06) | 1.06 (0.95-1.19) |
| **BMI,** kg/m² | 1.00 (0.98-1.01) | 1.00 (0.99-1.02) | 1.00 (0.98-1.02) | 1.00 (0.99-1.02) | 1.00 (0.99-1.02) | 1.00 (0.98-1.03) |
| **Sex** |  |  |  |  |  |  |
| Male | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Female | **1.85 (1.60-2.14)** | **1.87 (1.60-2.17)** | **1.75 (1.47-2.07)** | **1.86 (1.56-2.23)** | **1.95 (1.62-2.34)** | **1.87 (1.51-2.32)** |
| **Race** |  |  |  |  |  |  |
| White | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Mixed | 0.93 (0.79-1.09) | 0.91 (0.77-1.07) | 0.96 (0.80-1.16) | 0.87 (0.71-1.05) | 0.86 (0.70-1.05) | 0.88 (0.69-1.11) |
| Black | 0.94 (0.77-1.14) | 0.92 (0.75-1.13) | 0.95 (0.75-1.20) | 0.91 (0.72-1.16) | 0.94 (0.73-1.20) | 0.93 (0.70-1.23) |
| Others | 0.79 (0.54-1.16) | 0.79 (0.53-1.17) | 0.78 (0.49-1.23) | 0.80 (0.51-1.27) | 0.77 (0.48-1.25) | 0.65 (0.36-1.18) |
| **Education** |  |  |  |  |  |  |
| Lower | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Intermediate | 1.03 (0.82-1.29) | 1.06 (0.83-1.34) | 1.05 (0.80-1.39) | 1.11 (0.83-1.48) | 1.18 (0.86-1.60) | 1.25 (0.87-1.82) |
| Higher | 0.92 (0.73-1.16) | 0.96 (0.76-1.23) | 0.96 (0.73-1.27) | 0.97 (0.73-1.30) | 1.05 (0.77-1.43) | 1.06 (0.73-1.54) |
| **Alcohol intake** |  |  |  |  |  |  |
| None | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| No heavy drinking | 0.97 (0.84-1.12) | 0.94 (0.81-1.09) | 0.97 (0.81-1.15) | 0.92 (0.77-1.09) | 0.91 (0.76-1.09) | 0.93 (0.75-1.14) |
| Heavy drinking | 1.01 (0.76-1.35) | 0.97 (0.73-1.30) | 0.86 (0.61-1.22) | 1.03 (0.73-1.45) | 1.02 (0.72-1.45) | 0.83 (0.54-1.28) |
| **Smoking status** |  |  |  |  |  |  |
| Never | Ref. | Ref. | Ref. | Ref. | Ref. | Ref. |
| Former | 1.15 (0.99-1.34) | 1.11 (0.95-1.30) | 1.00 (0.84-1.21) | 1.05 (0.87-1.26) | 1.01 (0.83-1.23) | 0.90 (0.71-1.13) |
| Current | 1.09 (0.88-1.36) | 1.13 (0.90-1.40) | 1.04 (0.81-1.34) | 1.23 (0.95-1.58) | **1.31 (1.01-1.69)** | 1.25 (0.92-1.68) |

**Supplementary Table 4.** Sensitivity analyses of the association between potential determinants and persistent TPOAb positivity.

Legend: BMI: Body mass index. OR: odds ratio. 95%CI: 95% confidence interval. Statistically significant results are in bold.

Multivariate model adjusted for age, sex, BMI, race, education, smoking status, alcohol intake, rheumatic diseases, and TSH.

**Sensitivity analysis 1 -** Excluding participants using medication to treat thyroid diseases. **Sensitivity analysis 2 -** Plus excluding for the use of medications that interfere on thyroid function. **Sensitivity analysis 3 -** Plus excluding participants with abnormal thyroid function.

**Supplementary table 5.** Sensitivity analyses of the association between potential determinants and TPOAb categories.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **TPOAb categories** | | | |
|  | Undetectable  (≤ 5.00 IU/mL) | Low detectable (5.01-14.99 IU/mL) | High detectable (15.00-33.99 IU/mL) | Positive  (≥ 34.00 IU/mL) |
| **Age,** per 10 years |  |  |  |  |
| Sensitivity analysis 1 | Ref. | **0.91 (0.82-0.99)** | 0.91 (0.82-1.01) | 0.94 (0.84-1.05) |
| Sensitivity analysis 2 | Ref. | 0.91 (0.82-1.00) | 0.92 (0.82-1.03) | 0.93 (0.83-1.05) |
| Sensitivity analysis 3 | Ref. | 0.92 (0.83-1.02) | 0.93 (0.83-1.05) | 1.03 (0.91-1.17) |
| **BMI,** kg/m² |  |  |  |  |
| Sensitivity analysis 1 | Ref. | **1.03 (1.01-1.05)** | **1.02 (1.00-1.05)** | **1.03 (1.01-1.05)** |
| Sensitivity analysis 2 | Ref. | **1.03 (1.01-1.05)** | 1.02 (0.99-1.05) | **1.03 (1.01-1.06)** |
| Sensitivity analysis 3 | Ref. | **1.03 (1.00-1.05)** | 1.02 (0.99-1.04) | **1.03 (1.00-1.05)** |
| **Sex, female vs. male** |  |  |  |  |
| Sensitivity analysis 1 | Ref. | **1.28 (1.06-1.53)** | **1.35 (1.11-1.65)** | **2.16 (1.74-2.69)** |
| Sensitivity analysis 2 | Ref. | **1.24 (1.03-1.50)** | **1.33 (1.08-1.63)** | **2.21 (1.76-2.77)** |
| Sensitivity analysis 3 | Ref. | **1.23 (1.01-1.49)** | **1.33 (1.07-1.65)** | **2.13 (1.67-2.72)** |
| **Race, other vs. White** |  |  |  |  |
| Sensitivity analysis 1 | Ref. | 0.98 (0.56-1.71) | 1.02 (0.56-1.83) | 0.74 (0.39-1.42) |
| Sensitivity analysis 2 | Ref. | 1.08 (0.60-1.97) | 1.13 (0.60-2.13) | 0.80 (0.40-1.61) |
| Sensitivity analysis 3 | Ref. | 1.02 (0.56-1.87) | 1.12 (0.59-2.10) | 0.77 (0.38-1.60) |
| **Race, Black vs. White** |  |  |  |  |
| Sensitivity analysis 1 | Ref. | **0.37 (0.29-0.48)** | **0.33 (0.25-0.43)** | **0.35 (0.26-0.48)** |
| Sensitivity analysis 2 | Ref. | **0.39 (0.30-0.50)** | **0.34 (0.26-0.45)** | **0.37 (0.27-0.50)** |
| Sensitivity analysis 3 | Ref. | **0.40 (0.31-0.52)** | **0.35 (0.26-0.46)** | **0.39 (0.28-0.54)** |
| **Race, Mixed vs. White** |  |  |  |  |
| Sensitivity analysis 1 | Ref. | **0.39 (0.32-0.47)** | **0.35 (0.28-0.44)** | **0.36 (0.28-0.45)** |
| Sensitivity analysis 2 | Ref. | **0.40 (0.32-0.49)** | **0.37 (0.29-0.46)** | **0.36 (0.28-0.46)** |
| Sensitivity analysis 3 | Ref. | **0.42 (0.34-0.52)** | **0.39 (0.31-0.49)** | **0.41 (0.31-0.54)** |
| **Education, higher vs. lower** | | |  |  |
| Sensitivity analysis 1 | Ref. | **0.40 (0.29-0.56)** | **0.30 (0.21-0.42)** | **0.36 (0.25-0.53)** |
| Sensitivity analysis 2 | Ref. | **0.41 (0.29-0.59)** | **0.29 (0.20-0.42)** | **0.38 (0.25-0.56)** |
| Sensitivity analysis 3 | Ref. | **0.40 (0.28-0.58)** | **0.28 (0.19-0.41)** | **0.35 (0.23-0.54)** |
| **Education, intermediate vs. lower** | | |  |  |
| Sensitivity analysis 1 | Ref. | **0.61 (0.44-0.86)** | **0.55 (0.39-0.79)** | **0.59 (0.40-0.86)** |
| Sensitivity analysis 2 | Ref. | **0.62 (0.43-0.88)** | **0.54 (0.37-0.79)** | **0.60 (0.40-0.91)** |
| Sensitivity analysis 3 | Ref. | **0.62 (0.43-0.90)** | **0.53 (0.36-0.79)** | **0.59 (0.38-0.91)** |
| **Alcohol intake, heavy drinking vs. none** | |  |  |  |
| Sensitivity analysis 1 | Ref. | 0.76 (0.55-1.06) | 0.71 (0.50-1.02) | 0.68 (0.45-1.03) |
| Sensitivity analysis 2 | Ref. | **0.70 (0.50-0.98)** | **0.68 (0.47-0.98)** | **0.64 (0.42-0.97)** |
| Sensitivity analysis 3 | Ref. | 0.71 (0.51-1.00) | 0.69 (0.47-1.00) | **0.56 (0.35-0.89)** |
| **Alcohol intake, no heavy drinking vs. none** | | |  |  |
| Sensitivity analysis 1 | Ref. | 1.01 (0.84-1.22) | 1.05 (0.86-1.29) | 0.96 (0.77-1.19) |
| Sensitivity analysis 2 | Ref. | 0.97 (0.80-1.17) | 1.00 (0.81-1.23) | 0.92 (0.73-1.16) |
| Sensitivity analysis 3 | Ref. | 0.96 (0.79-1.17) | 0.97 (0.78-1.21) | 0.94 (0.74-1.21) |
| **Smoking status, current vs. never** | |  |  |  |
| Sensitivity analysis 1 | Ref. | **2.82 (1.89-4.20)** | **6.23 (4.14-9.37)** | **3.37 (2.18-5.22)** |
| Sensitivity analysis 2 | Ref. | **2.90 (1.92-4.40)** | **6.32 (4.14-9.66)** | **3.57 (2.27-5.62)** |
| Sensitivity analysis 3 | Ref. | **2.77 (1.83-4.20)** | **6.07 (3.96-9.31)** | **3.13 (1.96-5.01)** |
| **Smoking status, former vs. never** | |  |  |  |
| Sensitivity analysis 1 | Ref. | **1.22 (1.00-1.49)** | **1.29 (1.04-1.61)** | **1.31 (1.04-1.66)** |
| Sensitivity analysis 2 | Ref. | 1.20 (0.98-1.47) | **1.27 (1.02-1.60)** | 1.26 (0.99-1.61) |
| Sensitivity analysis 3 | Ref. | 1.20 (0.97-1.48) | **1.26 (1.00-1.60)** | 1.15 (0.89-1.50) |

Legend: BMI: Body mass index. OR: odds ratio. 95%CI: 95% confidence interval. Statistically significant results are in bold. Multivariate model adjusted for age, sex, BMI, race, education, smoking status, alcohol intake, rheumatic diseases, FT4 and TSH.

**Sensitivity analysis 1 -** Excluding participants using medication to treat thyroid diseases. **Sensitivity analysis 2 -** Plus excluding for the use of medications that interfere on thyroid function. **Sensitivity analysis 3 -** Plus excluding participants with abnormal thyroid function.

**Supplementary table 6.** Sensitivity analyses of the association (HR and 95%CI) of TPOAb and all-cause mortality risk.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **All-cause mortality** | | |
|  | **All** | **Male** | **Female** |
| **Sensitivity analysis 1** |  |  |  |
| TPOAb level (ln) | 1.04 (0.92-1.17) | 1.07 (0.91-1.26) | 0.99 (0.83-1.19) |
| TPOAb positivity | 0.98 (0.69-1.39) | 0.94 (0.58-1.51) | 1.03 (0.62-1.72) |
| TPOAb detectability | 1.19 (0.73-1.94) | 1.09 (0.62-1.90) | 1.58 (0.58-4.28) |
| Persistent TPOAb | 1.01 (0.62-1.65) | 0.98 (0.51-1.89) | 1.06 (0.50-2.23) |
| **Sensitivity analysis 2** |  |  |  |
| TPOAb level (ln) | 1.06 (0.93-1.20) | 1.10 (0.92-1.30) | 1.01 (0.84-1.23) |
| TPOAb positivity | 1.08 (0.75-1.55) | 1.03 (0.62-1.70) | 1.13 (0.66-1.92) |
| TPOAb detectability | 0.96 (0.59-1.56) | 0.85 (0.48-1.48) | 1.32 (0.48-3.58) |
| Persistent TPOAb | 1.20 (0.73-1.97) | 1.17 (0.61-2.25) | 1.26 (0.59-2.70) |
| **Sensitivity analysis 3** |  |  |  |
| TPOAb level (ln) | 1.11 (0.95-1.28) | 1.08 (0.87-1.33) | 1.13 (0.91-1.39) |
| TPOAb positivity | 1.16 (0.77-1.76) | 0.95 (0.51-1.74) | 1.42 (0.80-2.51) |
| TPOAb detectability | 0.92 (0.55-1.52) | 0.82 (0.46-1.47) | 1.22 (0.45-3.32) |
| Persistent TPOAb | 1.25 (0.70-2.21) | 1.03 (0.45-2.35) | 1.50 (0.67-3.34) |

Legend: Cox proportional hazards regression. HR: hazard ratio. Ln: natural log-transformed data. Statistically significant results are in bold. Persistent TPOAb refers to persistent TPOAb positivity in two visits.

Model 1 was adjusted for age, sex, and TSH. Model 2 was adjusted for age, sex, TSH, smoking status, BMI, hsCRP, diabetes mellitus, dyslipidemia, and hypertension.

**Sensitivity analysis 1 -** Excluding participants using medication to treat thyroid diseases. **Sensitivity analysis 2 -** Plus excluding for the use of medications that interfere on thyroid function. **Sensitivity analysis 3 -** Plus excluding participants with abnormal thyroid function.

**Supplementary table 7.** Sensitivity analyses of the association (HR and 95%CI) of TPOAb with cardiovascular, cancer-related and other-cause mortality risk.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Sensitivity analysis 1** | | | **Sensitivity analysis 2** | | | **Sensitivity analysis 3** | | |
|  | **All** | **Male** | **Female** | **All** | **Male** | **Female** | **All** | **Male** | **Female** |
| **Cardiovascular mortality** |  |  |  |  |  |  |  |  |  |
| TPOAb level | 0.84  (0.65-1.08) | 0.73  (0.49-1.11) | 0.95  (0.70-1.29) | 0.91  (0.69-1.18) | 0.82  (0.54-1.25) | 1.00  (0.72-1.38) | 0.94  (0.69-1.27) | 0.77  (0.51-1.17) | 1.12  (0.76-1.66) |
| TPOAb positivity | 0.61  (0.28-1.32) | 0.45  (0.13-1.59) | 0.80  (0.29-2.20) | 0.76  (0.35-1.65) | 0.59  (0.17-2.01) | 0.98  (0.35-2.76) | 0.79  (0.31-1.98) | 0.56  (0.13-2.34) | 1.08  (0.31-3.73) |
| TPOAb detectability | 0.83  (0.39-1.80) | 0.82  (0.33-2.04) | 0.88  (0.21-3.64) | 0.66  (0.30-1.43) | 0.64  (0.26-1.61) | 0.71  (0.17-2.94) | 0.72  (0.31-1.66) | 0.74  (0.27-2.03) | 0.68  (0.16-2.87) |
| Persistent TPOAb | 0.19  (0.02-1.46) | 0.29  (0.03-2.95) | 0.00  (0.00-0.00) | 0.23  (0.03-1.77) | 0.35  (0.04-3.43) | 0.00  (0.00-0.00) | 0.35  (0.05-2.58) | 0.62  (0.08-4.54) | 0.00  (0.00-0.00) |
| **Cancer-related mortality** |  |  |  |  |  |  |  |  |  |
| TPOAb level | 1.08  (0.91-1.28) | 1.23  (0.97-1.56) | 0.94  (0.73-1.21) | 1.08  (0.90-1.30) | 1.23  (0.95-1.59) | 0.95  (0.73-1.24) | 1.12  (0.90-1.39) | 1.20  (0.88-1.65) | 1.02  (0.75-1.37) |
| TPOAb positivity | 1.04  (0.61-1.79) | 1.23  (0.61-2.51) | 0.91  (0.41-2.04) | 1.09  (0.62-1.91) | 1.21  (0.57-2.58) | 1.01  (0.45-2.28) | 1.06  (0.55-2.03) | 0.90  (0.33-2.45) | 1.19  (0.49-2.87) |
| TPOAb detectability | 0.87  (0.44-1.70) | 0.73  (0.33-1.60) | 1.42  (0.34-5.95) | 0.74  (0.38-1.46) | 0.59  (0.27-1.30) | 1.26  (0.30-5.30) | 0.68  (0.34-1.35) | 0.56  (0.25-1.23) | 1.15  (0.27-4.86) |
| Persistent TPOAb | 1.42  (0.71-2.87) | 1.24  (0.45-3.38) | 1.66  (0.61-4.49) | 1.66  (0.82-3.35) | 1.43  (0.52-3.91) | 1.92  (0.69-5.34) | 1.40  (0.60-3.25) | 0.87  (0.21-3.60) | 1.92  (0.61-6.03) |
| **Other-cause mortality** |  |  |  |  |  |  |  |  |  |
| TPOAb level | **1.20**  **(1.03-1.40)** | **1.23**  **(1.00-1.51)** | 1.17  (0.89-1.54) | **1.22**  **(1.02-1.46)** | 1.25  (0.99-1.59) | 1.21  (0.90-1.62) | **1.27**  **(1.04-1.55)** | 1.23  (0.93-1.62) | **1.35**  **(1.01-1.82)** |
| TPOAb positivity | 1.32  (0.74-2.35) | 1.17  (0.54-2.54) | 1.64  (0.64-4.16) | 1.44  (0.77-2.70) | 1.34  (0.58-3.07) | 1.68  (0.59-4.81) | 1.71  (0.89-3.31) | 1.35  (0.55-3.33) | 2.35  (0.86-6.42) |
| TPOAb detectability | 6.81  (0.95-48.6) | 4.99  (0.70-35.6) | **27.1**  **(18.3-40.0)** | 5.36  (0.75-38.4) | 3.92  (0.54-28.2) | **27.4**  **(17.8-42.3)** | 4.60  (0.64-33.0) | 3.24  (0.45-23.4) | **45.5**  **(28.5-72.8)** |
| Persistent TPOAb | 1.32  (0.60-2.88) | 1.44  (0.52-3.99) | 1.18  (0.32-4.31) | 1.64  (0.75-3.61) | 1.84  (0.67-5.07) | 1.43  (0.39-5.28) | 1.89  (0.79-4.52) | 1.66  (0.49-5.65) | 2.31  (0.64-8.32) |

Legend: Fine-Gray subdistribution hazard regression. HR: hazard ratio. 95%CI: 95% confidence interval. Ln: natural log-transformed data. Statistically significant results are in bold. Persistent TPOAb refers to persistent TPOAb positivity in two visits.

Models were adjusted for age, sex, TSH, smoking status, BMI, hsCRP, diabetes mellitus, dyslipidemia, and hypertension.

Note: there was no women deceased in the cardiovascular mortality group after the exclusion for thyroid medication.

**Sensitivity analysis 1 -** Excluding participants using medication to treat thyroid diseases. **Sensitivity analysis 2 -** Plus excluding for the use of medications that interfere on thyroid function. **Sensitivity analysis 3 -** Plus excluding participants with abnormal thyroid function.