## Supplemental Tables

**Table S1.** General characteristics of hypothyroid patients with and without TRT

<table>
<thead>
<tr>
<th></th>
<th>TRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=6,897)</td>
<td>No (n=3,921)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>1,885 (27.3%)</td>
<td>1,392 (35.5%)</td>
</tr>
<tr>
<td>40-59</td>
<td>3,159 (45.8%)</td>
<td>1,686 (43.0%)</td>
</tr>
<tr>
<td>≥60</td>
<td>1,853 (26.9%)</td>
<td>843 (21.5%)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>49.9± 15.2</td>
<td>47.2± 15.6</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1,208 (17.5%)</td>
<td>737 (18.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>5,689 (82.5%)</td>
<td>3,184 (81.2%)</td>
</tr>
<tr>
<td>Income level (NTD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Financially dependent</td>
<td>1,356 (19.7%)</td>
<td>822 (21.0%)</td>
</tr>
<tr>
<td>15,840–29,999</td>
<td>3,312 (48.0%)</td>
<td>1,812 (46.2%)</td>
</tr>
<tr>
<td>30,000–44,999</td>
<td>1,242 (18.0%)</td>
<td>742 (18.9%)</td>
</tr>
<tr>
<td>≥45,000</td>
<td>987 (14.3%)</td>
<td>545 (13.9%)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>1.31± 1.90</td>
<td>1.18± 1.76</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1,632 (23.7%)</td>
<td>724 (18.5%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>802 (11.6%)</td>
<td>405 (10.3%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>128 (1.9%)</td>
<td>60 (1.5%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>313 (4.5%)</td>
<td>157 (4.0%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>170 (2.5%)</td>
<td>79 (2.0%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>554 (8.0%)</td>
<td>303 (7.7%)</td>
</tr>
<tr>
<td>COPD</td>
<td>322 (4.7%)</td>
<td>166 (4.2%)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>143 (2.1%)</td>
<td>68 (1.7%)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>57 (0.8%)</td>
<td>25 (0.6%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1,055 (15.3%)</td>
<td>467 (11.9%)</td>
</tr>
<tr>
<td>Fracture of lower limbs</td>
<td>70 (1.0%)</td>
<td>39 (1.0%)</td>
</tr>
<tr>
<td>Gout</td>
<td>191 (2.8%)</td>
<td>123 (3.1%)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>648 (9.4%)</td>
<td>136 (3.5%)</td>
</tr>
</tbody>
</table>

Continuous data are expressed as mean ± SD, and categorical data as numbers and percentages.

Abbreviations: COPD, chronic obstructive pulmonary disease; NTD, New Taiwan Dollar; SD, standard deviation; TRT, thyroxine replacement therapy.
Table S2. Comparison of venous thromboembolism risk between hypothyroid patients with and without thyroxine replacement therapy, stratified by age and sex

<table>
<thead>
<tr>
<th></th>
<th>Univariable model</th>
<th>Multivariable model†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude HR</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td>(95% CI)</td>
<td></td>
</tr>
<tr>
<td><strong>Age &lt; 40 years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT 1 (ref.) &amp; 1 (ref.)</td>
<td>0.32 (0.11–0.91)</td>
<td>0.033</td>
</tr>
<tr>
<td>With TRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 40–59 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT 1 (ref.) &amp; 1 (ref.)</td>
<td>0.62 (0.37–1.05)</td>
<td>0.077</td>
</tr>
<tr>
<td>With TRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 60 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT 1 (ref.) &amp; 1 (ref.)</td>
<td>0.98 (0.62–1.56)</td>
<td>0.935</td>
</tr>
<tr>
<td>With TRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT 1 (ref.) &amp; 1 (ref.)</td>
<td>1.64 (0.59–4.56)</td>
<td>0.34</td>
</tr>
<tr>
<td>With TRT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT 1 (ref.) &amp; 1 (ref.)</td>
<td>0.75 (0.53–1.05)</td>
<td>0.093</td>
</tr>
<tr>
<td>With TRT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The p value for interaction was 0.035 for evaluating the subgroup effect of age; the p value for interaction was 0.111 for evaluating the subgroup effect of sex.

†Multivariable Fine and Gray competing risk model with adjustments for all baseline characteristics listed in Table 1.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., reference; TRT, thyroxine replacement therapy.
<table>
<thead>
<tr>
<th>Hypothyroidism status</th>
<th>Events</th>
<th>Incidence rate*</th>
<th>Univariable model</th>
<th>Multivariable model†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Crude HR (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Adjusted HR (95% CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Non-hypothyroidism</td>
<td>134</td>
<td>95</td>
<td>1 (ref.)</td>
<td>1 (ref.)</td>
</tr>
<tr>
<td>Hypothyroidism overall</td>
<td>139</td>
<td>201</td>
<td>2.07 (1.64–2.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>1.77 (1.36–2.29)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Without TRT</td>
<td>64</td>
<td>238</td>
<td>2.44 (1.81–3.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>2.12 (1.52–2.97)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With TRT</td>
<td>75</td>
<td>177</td>
<td>1.84 (1.38–2.44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>1.44 (1.05–1.98)</td>
<td>0.025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism without TRT</td>
<td>64</td>
<td>238</td>
<td>1 (ref.)</td>
<td>1 (ref.)</td>
</tr>
<tr>
<td>Hypothyroidism with TRT</td>
<td>75</td>
<td>177</td>
<td>0.76 (0.54–1.06)</td>
<td>0.101</td>
</tr>
<tr>
<td></td>
<td>0.70 (0.50–0.98)</td>
<td>0.039</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The sensitivity analysis was performed by defining the index date as the third time of hypothyroidism diagnosis.

*per 100,000 person-years

†Multivariable Fine and Gray competing risk model with adjustments for all baseline characteristics listed in Table 1.

Abbreviations: CI, confidence interval; HR, hazard ratio; ref., reference; TRT, thyroxine replacement therapy.