Supplementary material to Ambrosino et al. “The risk of venous thromboembolism in patients with hepatitis C. A systematic review and meta-analysis” (Thromb Haemost 2016; 116.4)

<table>
<thead>
<tr>
<th>Suppl. Table 1</th>
<th>Transient risk factors for venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls in included studies.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suppl. Figure 1</td>
<td>PRISMA flow diagram.</td>
</tr>
<tr>
<td>Suppl. Figure 2</td>
<td>Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: analysis of adjusted risk estimates.</td>
</tr>
<tr>
<td>Suppl. Figure 3</td>
<td>Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: exclusion of studies specifically enrolling populations exposed to transient risk factors for VTE.</td>
</tr>
<tr>
<td>Suppl. Figure 4</td>
<td>Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: analysis of cohort studies.</td>
</tr>
<tr>
<td>Suppl. Figure 5</td>
<td>Funnel plots of effect size versus standard error for studies evaluating venous thromboembolism (VTE) in patients with HCV-infection and uninfected controls.</td>
</tr>
</tbody>
</table>
Suppl. Table 1. Transient risk factors for venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls in included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts (n)</th>
<th>Malignancy (%)</th>
<th>Pregnancy (%)</th>
<th>Hormonal therapy (%)</th>
<th>Orthopedic trauma/surgery (%)</th>
<th>Drug addiction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed 2012</td>
<td>HCV</td>
<td>47391</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>50291</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Best 2010</td>
<td>HCV</td>
<td>26444</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>8336822</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>El Bokl 2014</td>
<td>HCV</td>
<td>51</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>51</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Enger 2014</td>
<td>HCV</td>
<td>21919</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>67109</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RostamiJalilian2006</td>
<td>HCV</td>
<td>59</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>70</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>Wang 2015</td>
<td>HCV</td>
<td>3686</td>
<td>2.4</td>
<td>5.9</td>
<td>19.3</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>14744</td>
<td>3.9</td>
<td>6.9</td>
<td>23.3</td>
<td>3.2</td>
</tr>
</tbody>
</table>

HCV: hepatitis C virus.
Suppl. Figure 1. Prisma Flow Diagram.

* 3 studies on cirrhosis, 1 study without control group.
Suppl. Figure 2. Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: analysis of adjusted risk estimates.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed 2012</td>
<td>1,380</td>
<td>1,109</td>
<td>1,718</td>
<td>2,883</td>
<td>0.004</td>
</tr>
<tr>
<td>Best 2010 - DVT</td>
<td>2,643</td>
<td>2,364</td>
<td>2,955</td>
<td>17,073</td>
<td>0.000</td>
</tr>
<tr>
<td>Best 2010 - PE</td>
<td>3,584</td>
<td>3,228</td>
<td>3,980</td>
<td>23,887</td>
<td>0.000</td>
</tr>
<tr>
<td>Enger 2014 - DVT</td>
<td>1,220</td>
<td>0,800</td>
<td>1,860</td>
<td>0,924</td>
<td>0,356</td>
</tr>
<tr>
<td>Enger 2014 - PE</td>
<td>1,020</td>
<td>0,601</td>
<td>1,732</td>
<td>0,073</td>
<td>0,942</td>
</tr>
<tr>
<td>Wang 2015 - DVT</td>
<td>1,960</td>
<td>1,030</td>
<td>3,730</td>
<td>2,050</td>
<td>0,040</td>
</tr>
<tr>
<td>Wang 2015 - PE</td>
<td>2,100</td>
<td>0,876</td>
<td>5,036</td>
<td>1,663</td>
<td>0,096</td>
</tr>
<tr>
<td>Overall Effect</td>
<td>1,876</td>
<td>1,326</td>
<td>2,654</td>
<td>3,553</td>
<td>0,000</td>
</tr>
</tbody>
</table>

\(P^2: 93.4\%, p < 0.001\)

95% CI: 95% confidence interval; HCV: hepatitis C virus; DVT: deep venous thrombosis; PE: pulmonary embolism.
Suppl. Figure 3. Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: exclusion of studies specifically enrolling populations exposed to transient risk factors for VTE.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed 2012 - DVT</td>
<td>1.190</td>
<td>0.908</td>
<td>1.561</td>
<td>1.259</td>
<td>0.208</td>
</tr>
<tr>
<td>Ahmed 2012 - PE</td>
<td>1.428</td>
<td>1.007</td>
<td>2.025</td>
<td>2.002</td>
<td>0.045</td>
</tr>
<tr>
<td>El Bokl 2014 - DVT</td>
<td>12.183</td>
<td>0.656</td>
<td>226.356</td>
<td>1.677</td>
<td>0.094</td>
</tr>
<tr>
<td>Enger 2014 - DVT</td>
<td>1.987</td>
<td>1.363</td>
<td>2.897</td>
<td>3.571</td>
<td>0.000</td>
</tr>
<tr>
<td>Enger 2014 - PE</td>
<td>1.015</td>
<td>0.632</td>
<td>1.628</td>
<td>0.060</td>
<td>0.952</td>
</tr>
<tr>
<td>Wang 2015 - DVT</td>
<td>2.073</td>
<td>1.110</td>
<td>3.871</td>
<td>2.289</td>
<td>0.022</td>
</tr>
<tr>
<td>Wang 2015 - PE</td>
<td>2.002</td>
<td>0.856</td>
<td>4.682</td>
<td>1.602</td>
<td>0.109</td>
</tr>
<tr>
<td>Overall Effect</td>
<td>1.493</td>
<td>1.167</td>
<td>1.910</td>
<td>3.191</td>
<td>0.001</td>
</tr>
</tbody>
</table>

I^2: 44.1%, p = 100

Lower in HCV  Higher in HCV

95% CI: 95% confidence interval; HCV: hepatitis C virus; DVT: deep venous thrombosis; PE: pulmonary embolism.
Figure 4. Sensitivity analysis. Risk of venous thromboembolism (VTE) in hepatitis C virus-infected subjects and uninfected controls: analysis of studies with a retrospective design.

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed 2012 - DVT</td>
<td>1.190</td>
<td>0.908</td>
<td>1.561</td>
<td>1.259</td>
<td>0.208</td>
</tr>
<tr>
<td>Ahmed 2012 - PE</td>
<td>1.428</td>
<td>1.007</td>
<td>2.025</td>
<td>2.002</td>
<td>0.045</td>
</tr>
<tr>
<td>Best 2010 - DVT</td>
<td>2.414</td>
<td>2.160</td>
<td>2.698</td>
<td>15.541</td>
<td>0.000</td>
</tr>
<tr>
<td>Best 2010 - PE</td>
<td>3.533</td>
<td>3.187</td>
<td>3.917</td>
<td>23.978</td>
<td>0.000</td>
</tr>
<tr>
<td>El Bokl 2014 - DVT</td>
<td>12.183</td>
<td>6.656</td>
<td>22.6356</td>
<td>1.677</td>
<td>0.094</td>
</tr>
<tr>
<td>Enger 2014 - DVT</td>
<td>1.987</td>
<td>1.363</td>
<td>2.897</td>
<td>3.571</td>
<td>0.000</td>
</tr>
<tr>
<td>Enger 2014 - PE</td>
<td>1.015</td>
<td>0.632</td>
<td>1.628</td>
<td>0.060</td>
<td>0.952</td>
</tr>
<tr>
<td>Wang 2015 - DVT</td>
<td>2.073</td>
<td>1.110</td>
<td>3.871</td>
<td>2.289</td>
<td>0.022</td>
</tr>
<tr>
<td>Wang 2015 - PE</td>
<td>2.002</td>
<td>0.856</td>
<td>4.682</td>
<td>1.602</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>Overall Effect</strong></td>
<td>1.890</td>
<td>1.375</td>
<td>2.597</td>
<td>3.926</td>
<td>0.000</td>
</tr>
</tbody>
</table>

F: 91.8%, p < 0.001

95% confidence interval; HCV: hepatitis C virus; DVT: deep venous thrombosis; PE: pulmonary embolism.
Suppl. Figure 5. Funnel plots of effect size versus standard error for studies evaluating venous thromboembolism (VTE) in patients with HCV-infection and uninfected controls.

Egger’s p = 0.128