

## **Supplementary Material**

### **Table of Contents**

|   |    |
|---|----|
| Supplementary Table 1 – Search strategies .....   | 2  |
| Supplementary Table 2. Blinding Index of patients in included trials.....   | 3  |
| Supplementary Table 3. Metaregression according to age, male (%), diabetic patients (%), .....<br>number of anti-hypertensive drugs ..... | 4  |
| Supplementary Figure 1. Jackknife leave-one-out sensitivity analysis .....  | 5  |
| Supplementary Figure 2. Subgroup analysis according to risk of bias.....  | 7  |
| Supplementary Figure 3. Subgroup analysis by generation of procedure.....   | 9  |
| Supplementary Figure 4. Funnel plot for primary outcomes.....   | 11 |

**Supplementary Table 1 – Search strategies**

| #         | <u>Searches</u>                 |
|-----------|---------------------------------|
| <b>1</b>  | (renal adj2 denervation).af.    |
| <b>2</b>  | randomized controlled trial.pt. |
| <b>3</b>  | controlled clinical trial.pt.   |
| <b>4</b>  | randomized.ab.                  |
| <b>5</b>  | sham.ab.                        |
| <b>6</b>  | randomly.ab.                    |
| <b>7</b>  | trial.ab.                       |
| <b>8</b>  | exp animals/ not humans.sh.     |
| <b>9</b>  | 2 or 3 or 4 or 5 or 6 or 7      |
| <b>10</b> | 9 not 8                         |
| <b>11</b> | 1 and 10                        |
| <b>12</b> | sham.af.                        |
| <b>13</b> | sham*.af.                       |
| <b>14</b> | sham-control*.af.               |
| <b>15</b> | 12 or 13 or 14                  |
| <b>16</b> | 11 and 15                       |
| <b>17</b> | remove duplicates from 16       |

**Supplementary Table 2. Blinding Index of patients in included trials**

|                               |                   | SYMPPLICITY HTN-3 | Desch et al. | ReSet | RADIANCE-HTN SOLO                     | SPYRAL HTN-OFF MED Pivotal | SPYRAL HTN-ON MED | REDUCE HTN: REINFORCE | RE |
|-------------------------------|-------------------|-------------------|--------------|-------|---------------------------------------|----------------------------|-------------------|-----------------------|----|
| <b>James Blinding Index *</b> | Discharge         | 0,68 [0,64; 0,72] | -            | 0,83  | 0,7 [0,62; 0,77]                      | 0,66 [0,61; 0,71]          | 0,78 [0,70; 0,85] | 0,64 [0,51; 0,78]     |    |
|                               | Maximum follow-up | 0,77 [0,74; 0,81] | -            | -     | 0,6 [0,52; 0,68]                      | 0,53 (0,48; 0,59)          | 0,64 [0,54; 0,74] | 0,56 [0,42; 0,70]     |    |
| <b>Bang Blinding Index **</b> |                   |                   |              |       | <b>RSD Sham</b>                       |                            |                   |                       |    |
|                               | Discharge         | -                 | -            | -     | 0,30 [0,16; 0,44] -0,01 [-0,17; 0,14] | -                          | -                 | -                     |    |
|                               | Maximum follow-up | -                 | -            | -     | 0,24 [0,08; 0,41] 0,18 [0,01; 0,35]   | -                          | -                 | -                     |    |

RSD – Renal Sympathetic Denervation

\* Confidence intervals superior to and excluding 0,50 indicate effective blinding.<sup>28</sup>

\*\* Values approaching zero indicate effective blinding. Values approaching either 1 or -1 indicate incomplete blinding.<sup>29</sup>

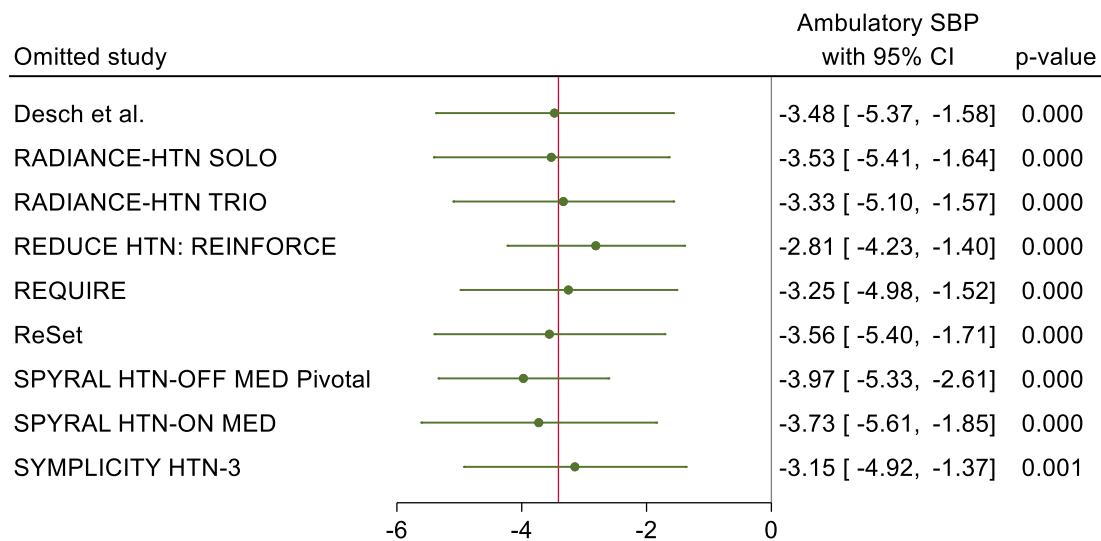
**Supplementary Table 3. Metaregression according to age, male (%), diabetic patients (%),****number of anti-hypertensive drugs**

| Variable              | Coefficient | Standard error | P>z   | [95% conf. | interval] |
|-----------------------|-------------|----------------|-------|------------|-----------|
| <b>Ambulatory SBP</b> |             |                |       |            |           |
| Age                   | -.2824554   | 0.4196696      | 0.501 | -1.104993  | .5400819  |
| Male (%)              | -.0403876   | .1119416       | 0.718 | -.259789   | .1790139  |
| Diabetes (%)          | -.0729278   | .0504913       | 0.149 | -.171889   | .0260333  |
| Drugs                 | -.2166692   | .4170695       | 0.603 | -1.03411   | .6007721  |
| <b>Ambulatory DBP</b> |             |                |       |            |           |
| Age                   | -.3167957   | .1807991       | 0.080 | -.6711554  | .0375641  |
| Male (%)              | .0108073    | .0601088       | 0.857 | -.1070038  | .1286184  |
| Diabetes (%)          | -.0543901   | .0185257       | 0.003 | -.0906999  | -.0180803 |
| Drugs                 | -.3277363   | .1495818       | 0.028 | -.6209113  | -.0345613 |
| <b>Office SBP</b>     |             |                |       |            |           |
| Age                   | -1.731316   | .5721542       | 0.002 | -2.852717  | -.609914  |
| Male (%)              | .063492     | .148603        | 0.669 | -.2277646  | .3547485  |
| Diabetes (%)          | -.1598503   | .0654515       | 0.015 | -.2881328  | -.0315677 |
| Drugs                 | -1.154066   | .6512575       | 0.076 | -2.430508  | .122375   |
| <b>Office DBP</b>     |             |                |       |            |           |
| Age                   | -.7335358   | .4019761       | 0.068 | -1.521395  | .054323   |
| Male (%)              | -.0182236   | .0632087       | 0.773 | -.1421103  | .1056631  |
| Diabetes (%)          | -.0662281   | .0417557       | 0.113 | -.1480678  | .0156117  |
| Drugs                 | -.4408458   | .333437        | 0.186 | -1.09437   | .2126787  |

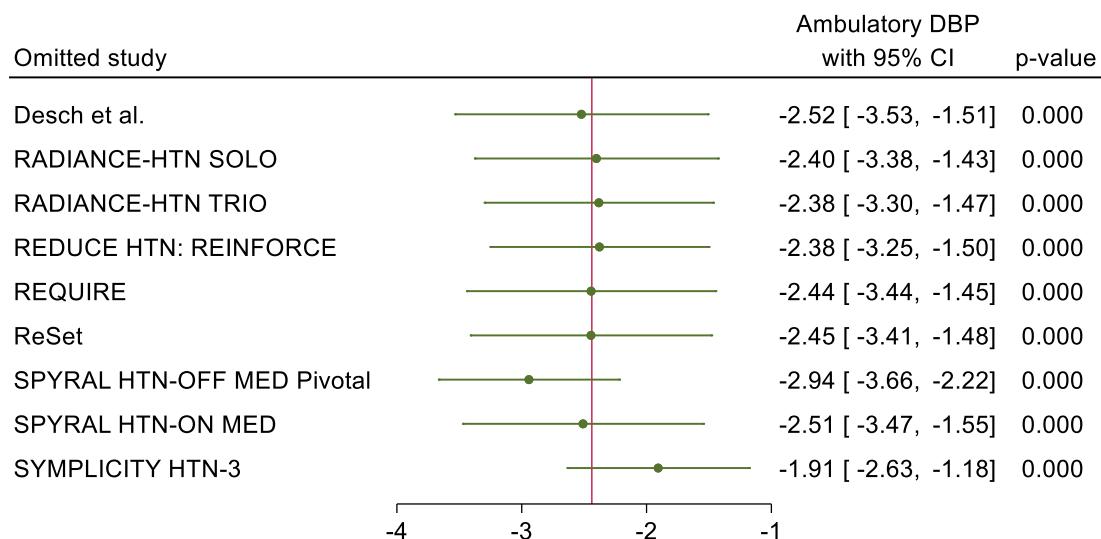
SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; Conf. interval – Confidence interval

**Supplementary Figure 1. Jackknife leave-one-out sensitivity analysis**

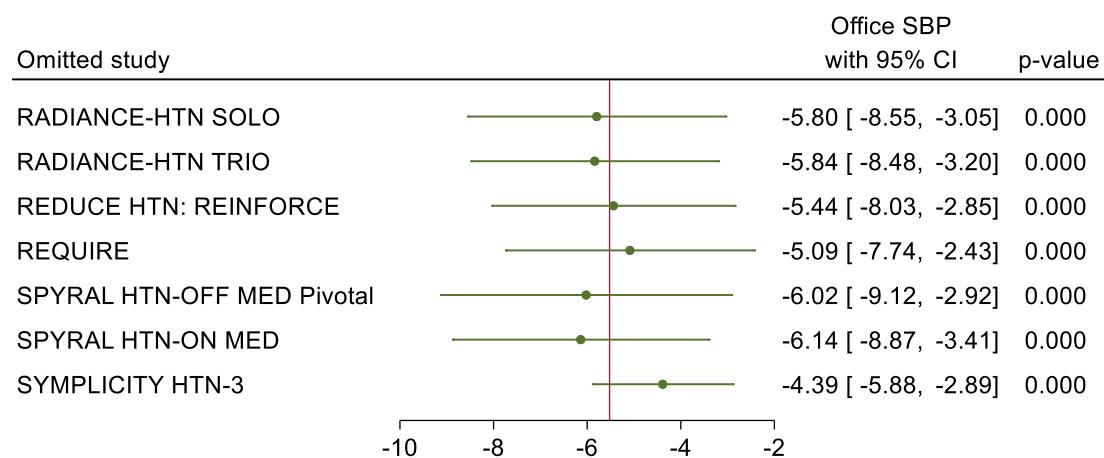
**(A) Change in Ambulatory Systolic Blood Pressure**



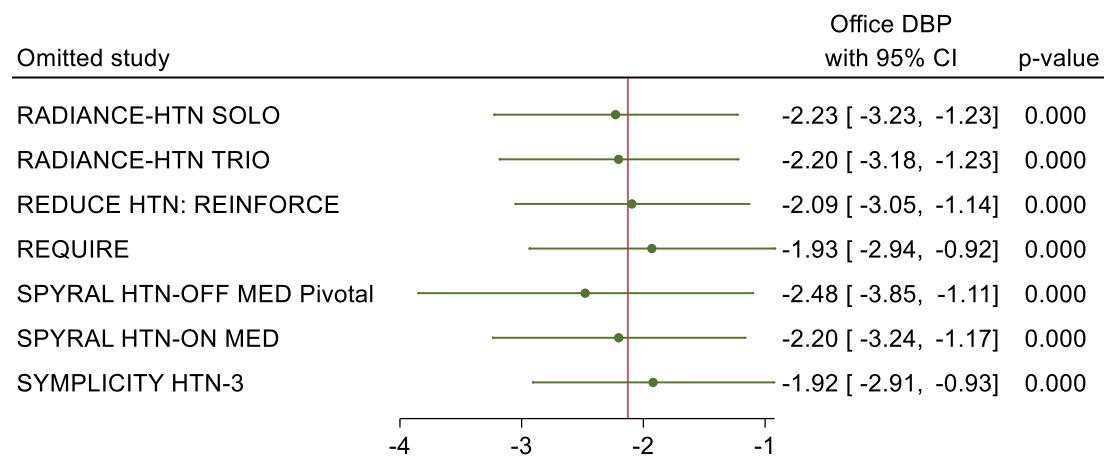
**(B) Change in Ambulatory Diastolic Blood Pressure**



**(C) Change in Office Systolic Blood Pressure**



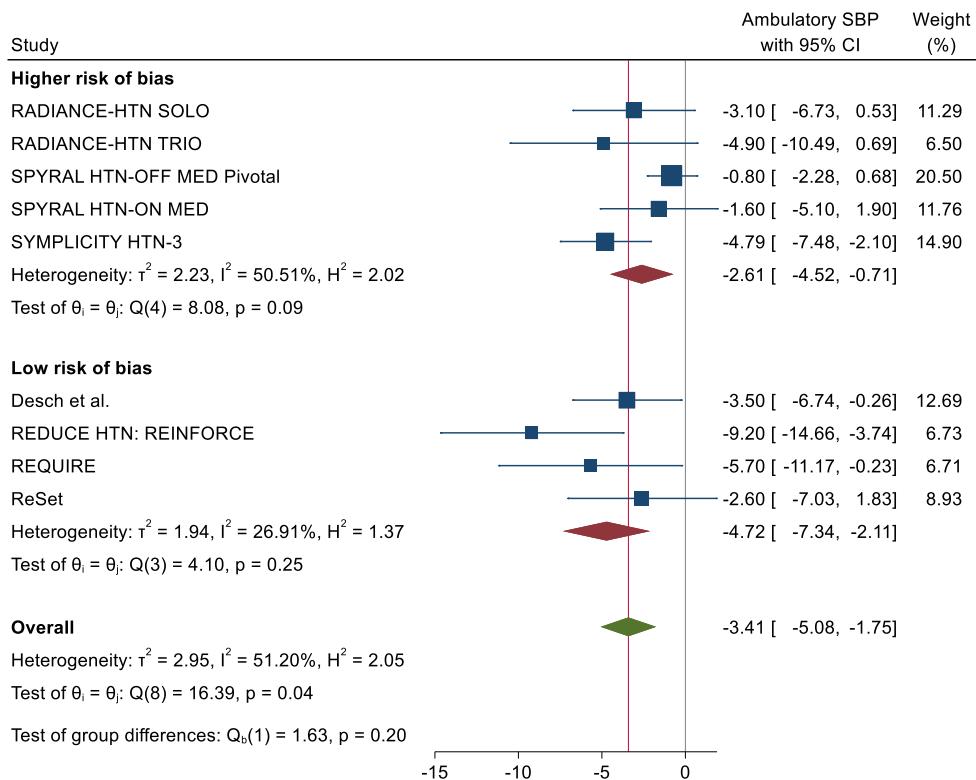
**(D) Change in Office Diastolic Blood Pressure**



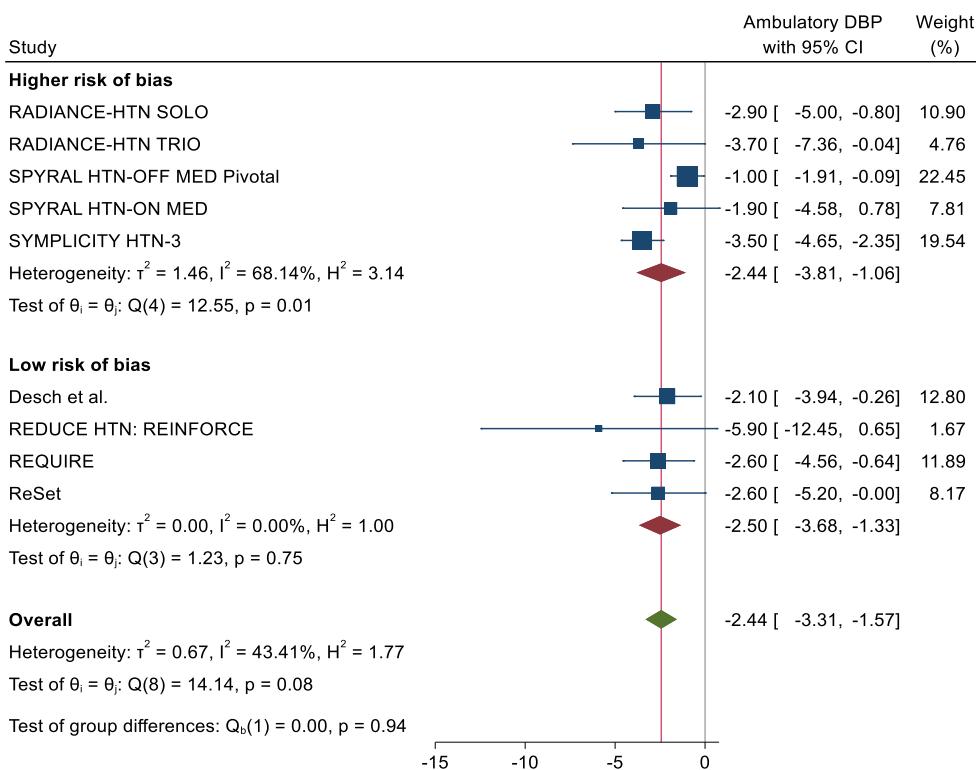
SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; CI – Confidence Interval

## Supplementary Figure 2. Subgroup analysis according to risk of bias.

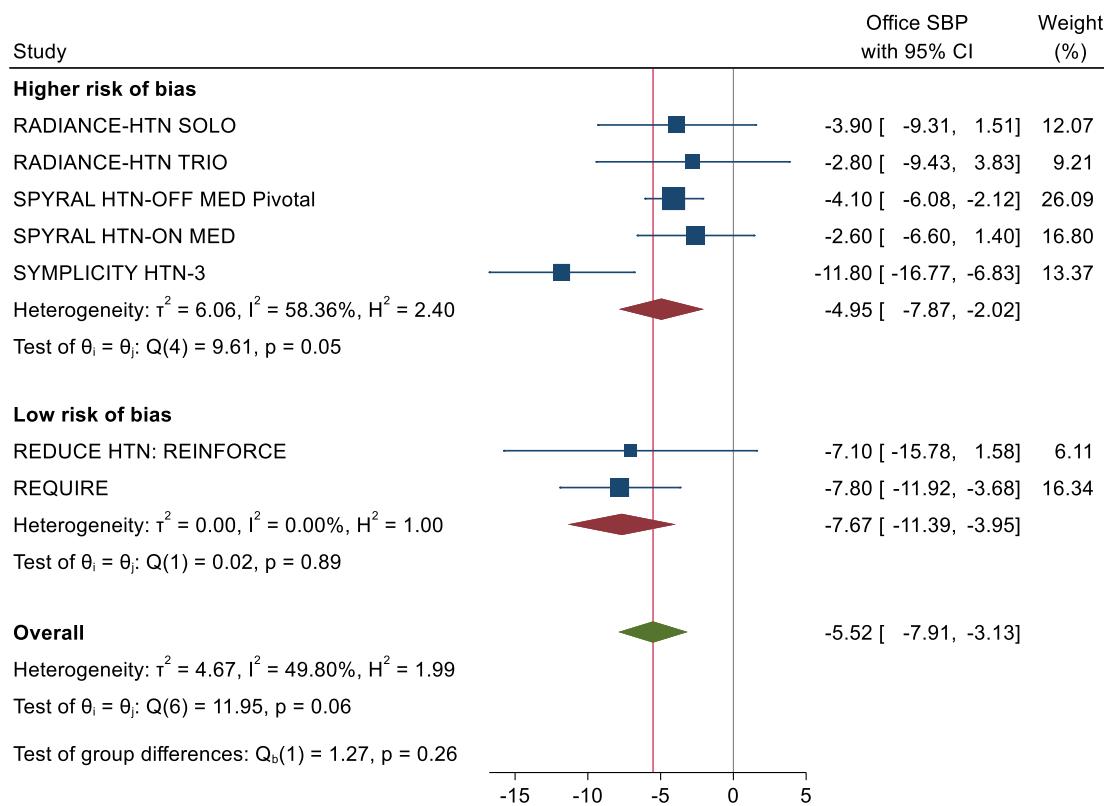
### (A) Change in Ambulatory Systolic Blood Pressure (SBP)



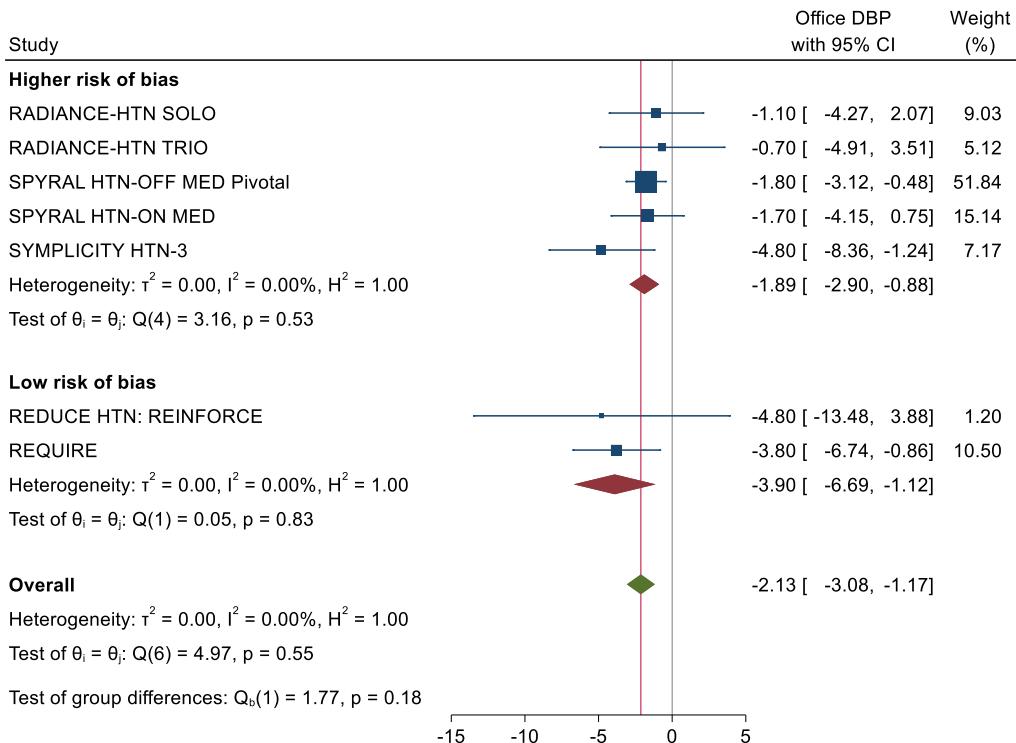
### (B) Change in Ambulatory Diastolic Blood Pressure (DBP)



### (C) Change in Office Systolic Blood Pressure (SBP)



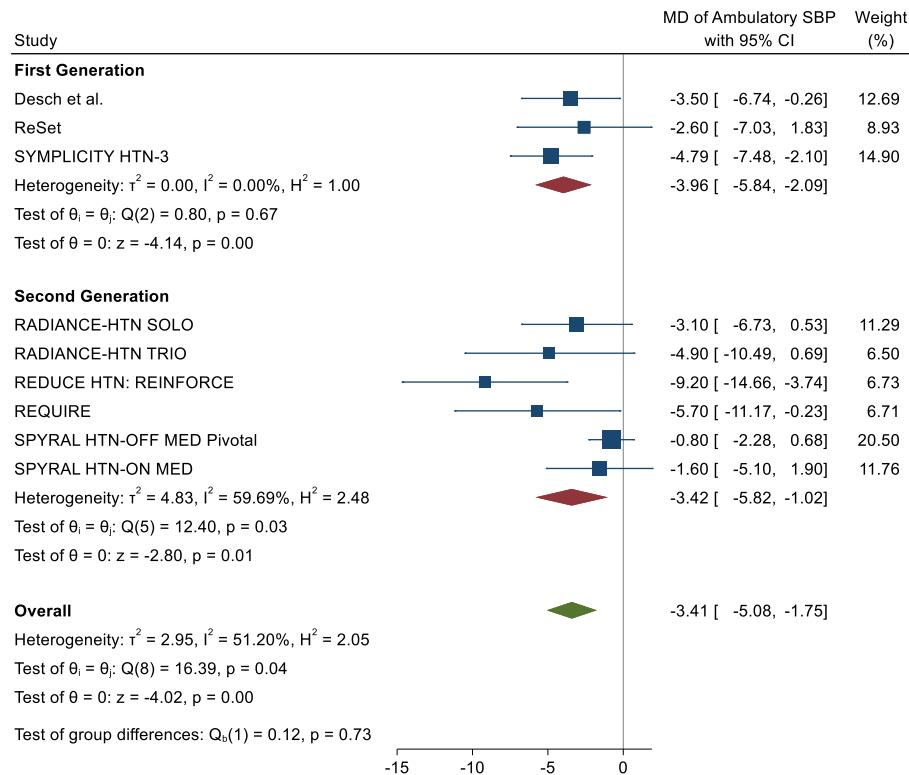
### (D) Change in Office Diastolic Blood Pressure (DBP)



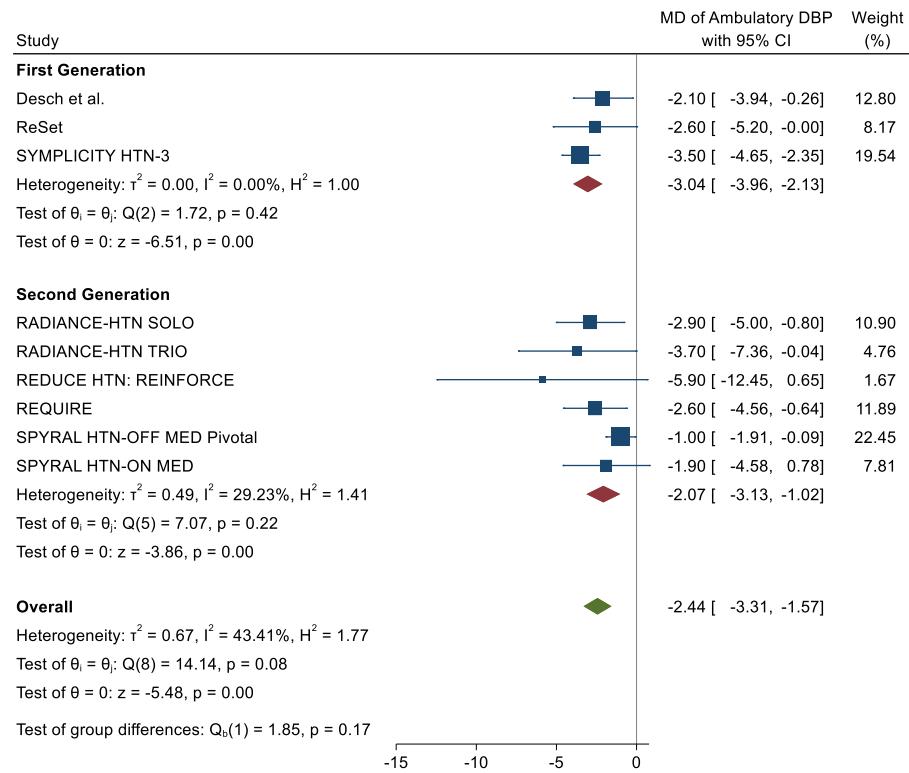
SBP – Systolic Blood Pressure; DBP – Diastolic Blood Pressure; CI – Confidence Interval

### **Supplementary Figure 3. Subgroup analysis by generation of procedure**

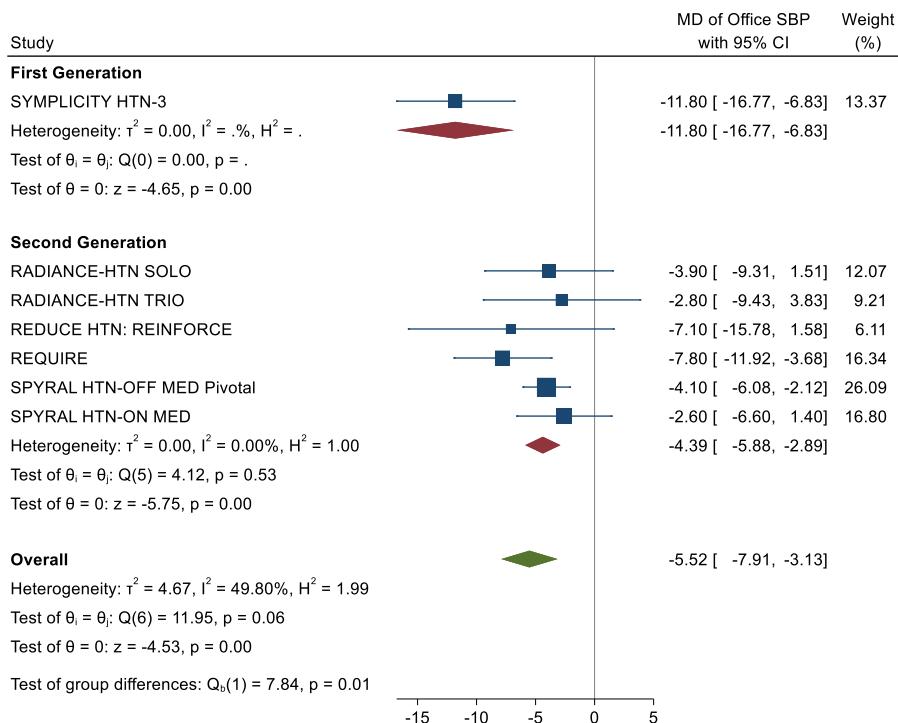
#### **(A) Change in Ambulatory Systolic Blood Pressure**



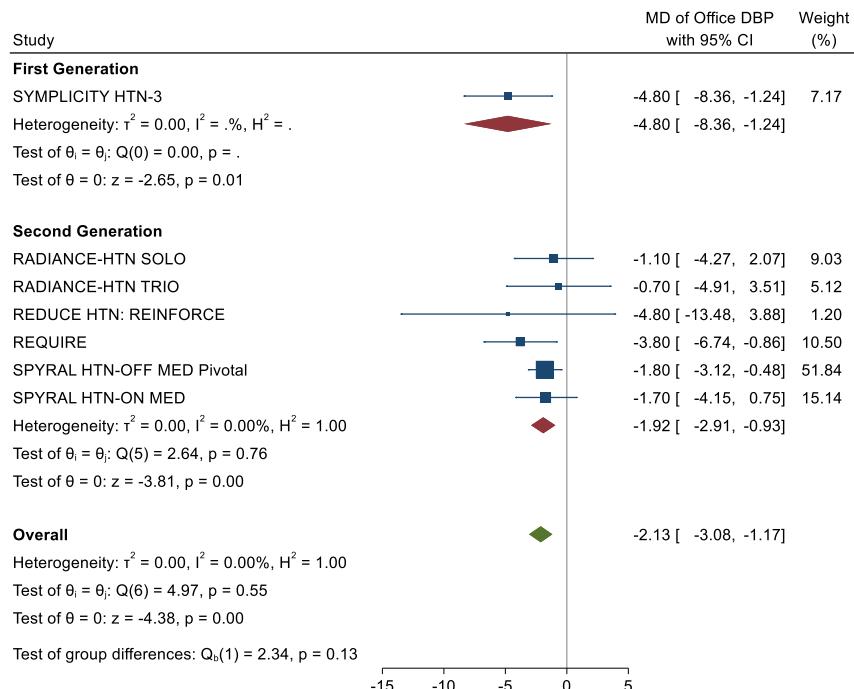
#### **(B) Change in Ambulatory Diastolic Blood Pressure**



### (C) Change in Office Systolic Blood Pressure



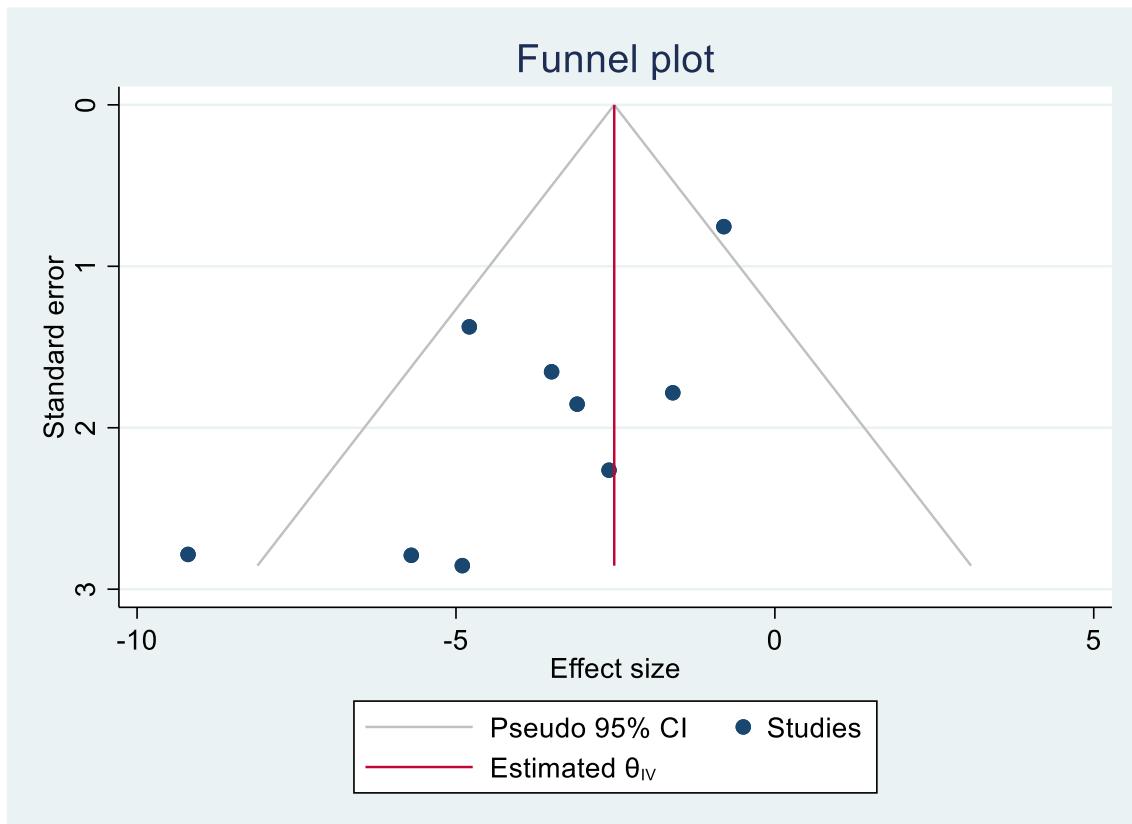
### (D) Change in Office Diastolic Blood Pressure



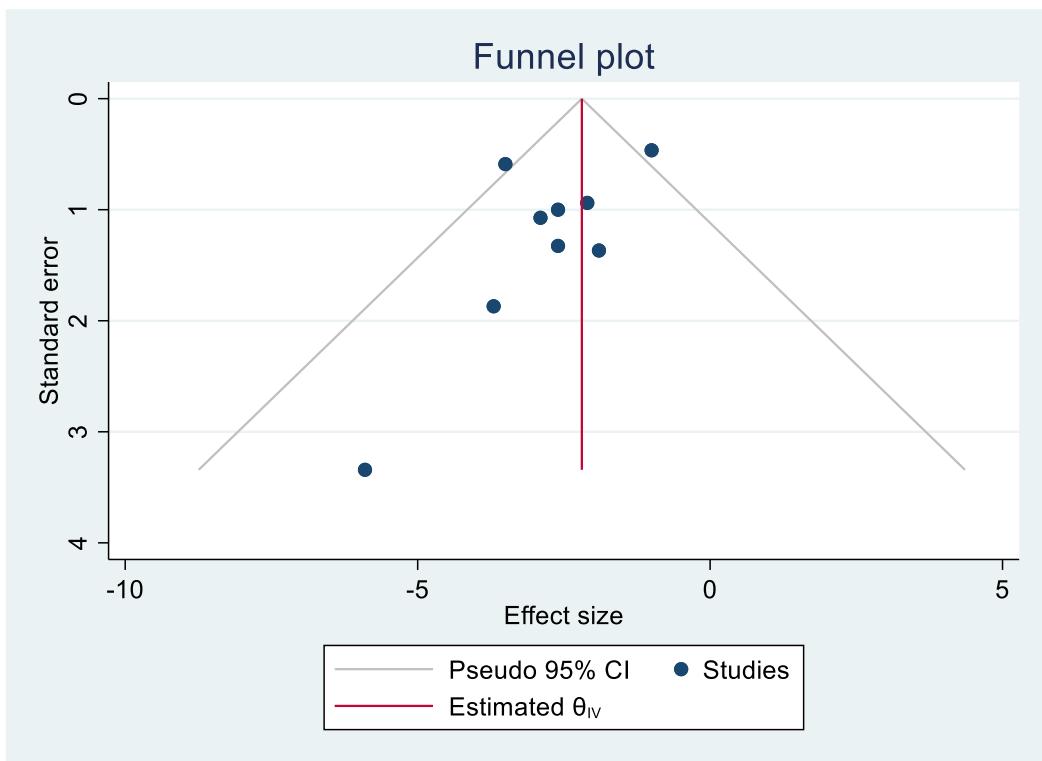
BP - Blood Pressure; RD - Renal Denervation; CI - Confidence Interval; IV - Inverse Variance;

**Supplementary Figure 4. Funnel plot for primary outcomes**

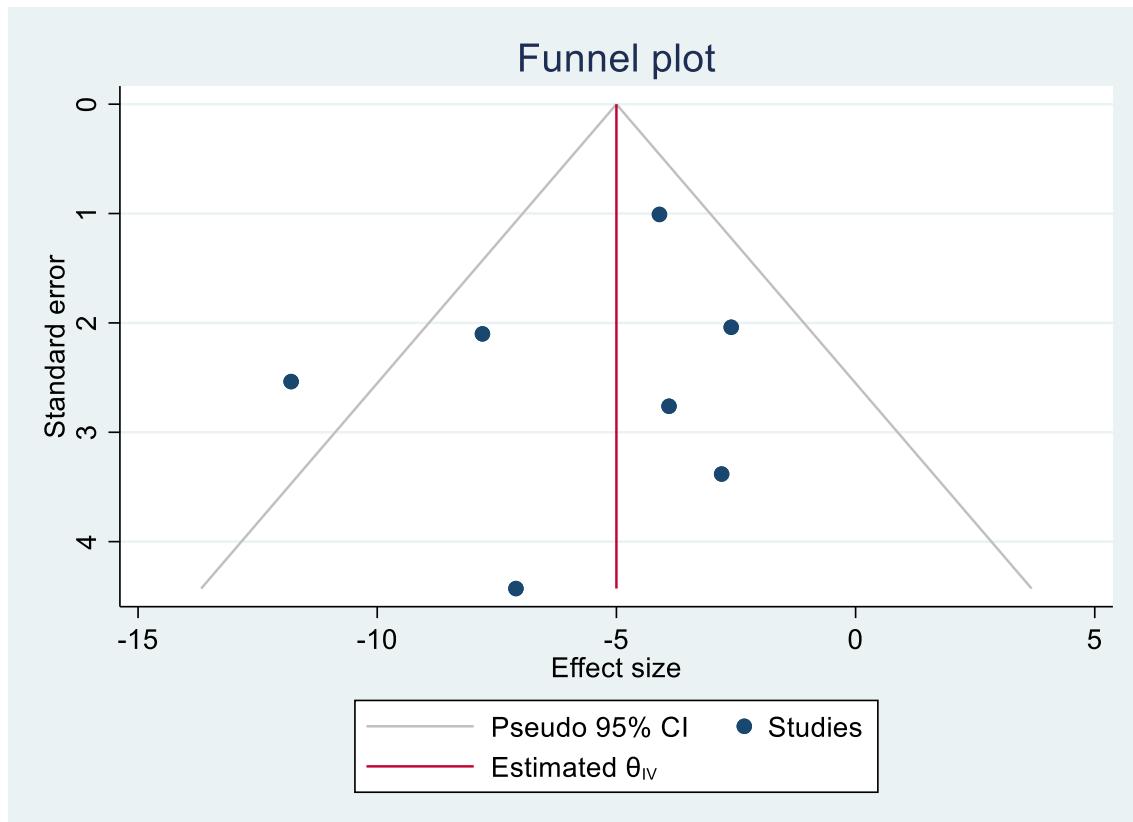
**(A) Ambulatory Systolic Blood Pressure ( $P = 0.0016$ )**



**(B) Ambulatory Diastolic Blood Pressure ( $P = 0.1900$ )**



**(C) Funnel plot for Office Systolic Blood Pressure ( $P = 0.6677$ )**



**(D) Funnel plot for Office Diastolic Blood Pressure ( $P = 0.3889$ )**

