

**Supplementary Table 1. Search Strategy**

|                                   |  |
|-----------------------------------|--|
| PubMed/MEDLINE<br>(41 results)    | ("semaglutide"[Supplementary Concept] OR "semaglutide"[All Fields]) AND ("obese"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields]) AND "HFpEF"[All Fields] |
| Cochrane Library<br>(22 results)  | Semaglutide AND Obesity AND HFpEF  |
| Google Scholar<br>(1,306 results) | Semaglutide AND Obesity AND HFpEF  |
| Science Direct<br>(233 results)   | Semaglutide AND Obesity AND HFpEF  |
| Clinicaltrials.gov<br>(3 results) | Semaglutide AND Obesity AND HFpEF  |

**Supplementary Table 2(a): Risk of Bias assessment**

|                | Bias  | Risk of Bias | Author Judgement  |
|----------------|---|--------------|---|
| Kosiborod 2023 | Random sequence generation (selection bias) | Low Risk     | Participants were randomly allocated in a 1:1 ratio utilizing an interactive web-based response system, which ensured the randomization process was automated and unbiased, providing equal probability for assignment to each study group.           |
|                | Allocation concealment (selection bias)     | Low Risk     | The study utilized stratified randomization according to baseline BMI, ensuring an even distribution of participants between treatment groups, which reduced the potential for selection bias and strengthened the internal validity of the findings. |

|  |   |          |  |
|--|---|----------|--|
|  | Blinding of participants and personnel (performance bias) | Low Risk | As a double-blind trial, both participants and investigators were unaware of group assignments, significantly lowering the risk of performance bias.                                     |
|  | Blinding of outcome assessment (detection bias)           | Low Risk | While explicit details are lacking, the trial's design and methods indicate a low risk of detection bias, presumably due to the effective blinding of outcome assessors.                 |
|  | Incomplete outcome data (attrition bias)                  | Low Risk | With minimal dropout rates and thorough analysis of participants lost to follow-up, the study effectively managed and reported attrition, thereby minimizing the risk of attrition bias. |
|  | Selective reporting (Reporting bias)                      | Low Risk | The study reported all outcomes as initially planned, with no signs of selective reporting.  |
|  | Other bias  | Low Risk | The study followed strict methodological guidelines and protocols, with no evidence of additional sources of bias impacting the results, indicating a low risk of other bias.            |

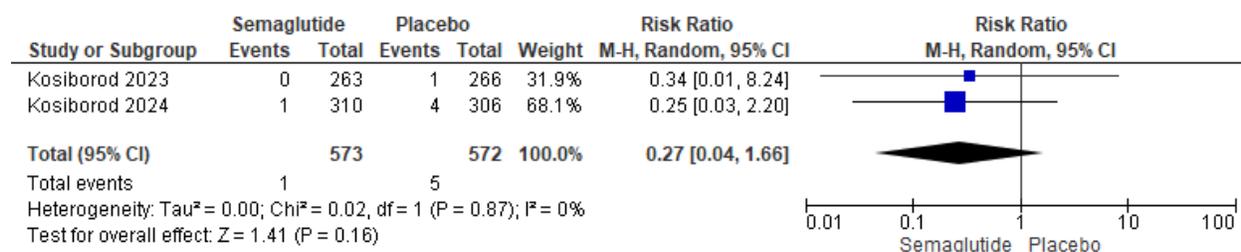
|                | Bias  | Risk of Bias | Author Judgement   |
|----------------|---|--------------|--|
| Kosiborod 2024 | Random sequence generation (selection bias)               | Low Risk     | By using stratified randomization based on BMI, the study ensured an even distribution of participants across groups, effectively reducing the risk of selection bias.   |
|                | Allocation concealment (selection bias)                   | Low Risk     | The study employed stratified randomization based on baseline BMI, achieving balanced participant distribution across treatment groups, which diminished the risk of selection bias and enhanced the internal validity of the results. |
|                | Blinding of participants and personnel (performance bias) | Low Risk     | Being a double-blind trial, it ensured that both participants and investigators were blinded to group assignments.   |
|                | Blinding of outcome assessment (detection bias)           | Low Risk     | Although specific details are not provided, the trial's design and methods suggest a low risk of detection bias, likely due to the effective blinding of outcome assessors.  |
|                | Incomplete outcome data (attrition bias)                  | Low Risk     | With low dropout rates and a comprehensive analysis of participants lost to follow-up, the study effectively handled and reported attrition, thereby reducing the risk of attrition bias.  |
|                | Selective reporting (Reporting bias)                      | Low Risk     | The study reported all outcomes as originally planned, without evidence of selective reporting.  |

|  |            |          |   |
|--|------------|----------|---|
|  | Other bias | Low Risk | The study adhered to rigorous methodological guidelines and protocols, showing no evidence of additional biases affecting the results, which suggests a low risk of other bias. |
|--|------------|----------|---|

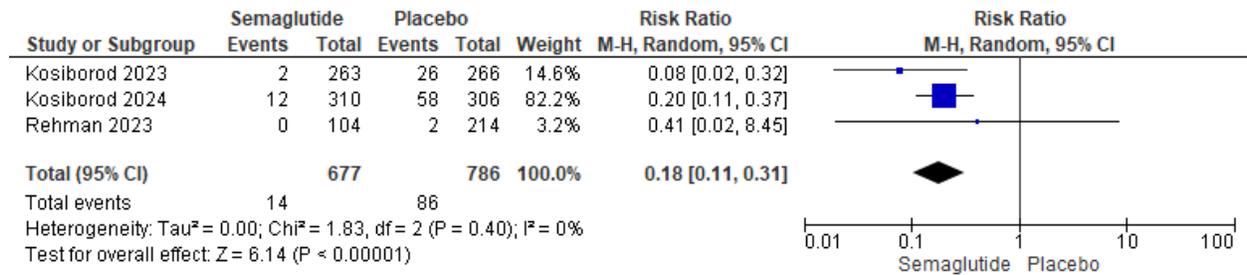
**Supplementary Table 2(b):** Newcastle-Ottawa quality assessment scale for cohort studies

|  | Study name  |
|--|-------------|
|  | Rehman 2023 |
| <b>Selection (4)</b>   |             |
| Representativeness of the exposed cohort                                 | *           |
| Selection of the non-exposed cohort                                      | *           |
| Ascertainment of exposure  | *           |
| Demonstration that outcome of interest was not present at start of study | *           |
| <b>Comparability (2)</b>   |             |
| Comparability of cohorts on the basis of the design or analysis          | **          |
| <b>Outcome (3)</b>   |             |
| Assessment of outcome  | *           |
| Was follow-up long enough for outcomes to occur                          | *           |
| Adequacy of follow up of cohorts   | *           |
| <b>Total (9)</b>   | <b>9</b>    |

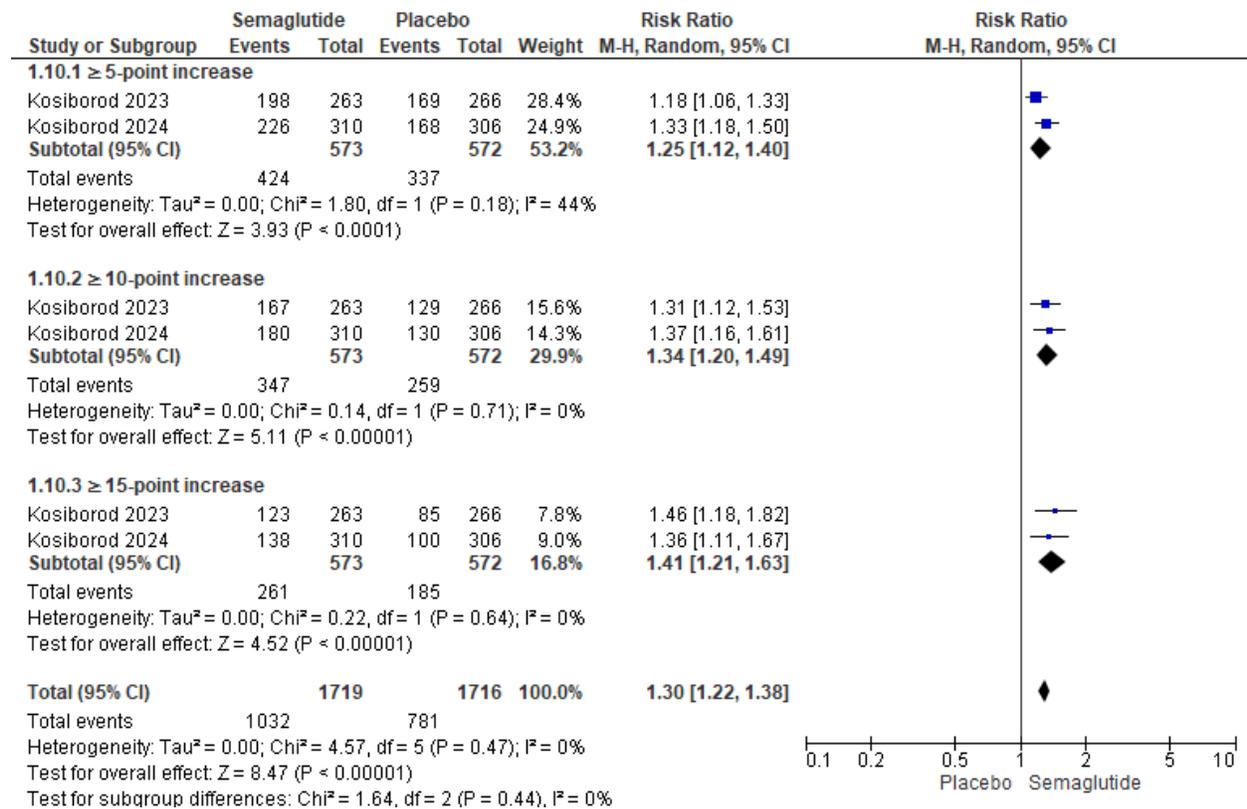
**Supplementary Figure 1.** Forest plot of Death from cardiovascular causes



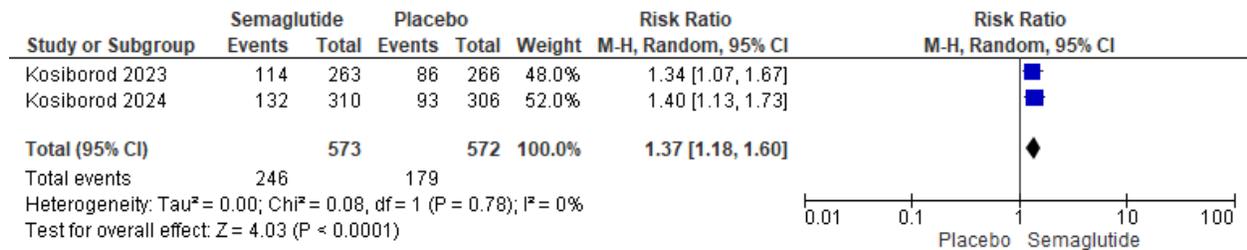
**Supplementary Figure 2: Forest plot of Heart failure events**



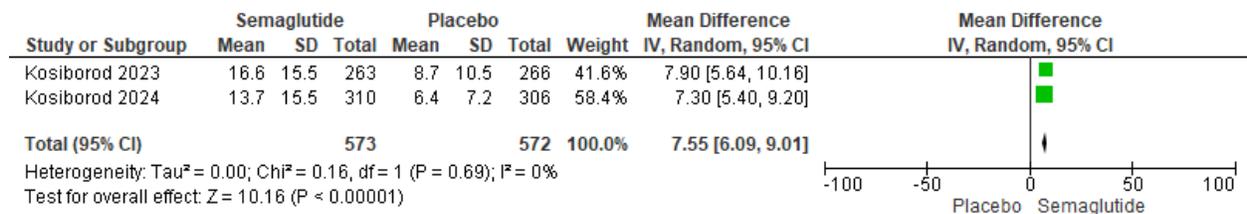
**Supplementary Figure 3: Forest plot of Increase in KCCQ-CSS at week 52**



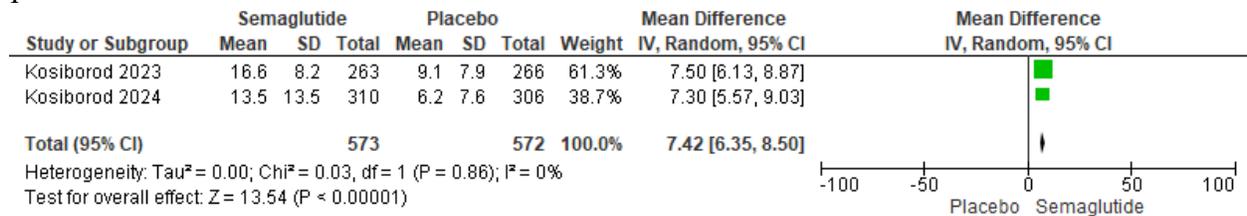
**Supplementary Figure 4:** Forest plot of Attainment of anchor-based threshold for change in KCCQ-CSS



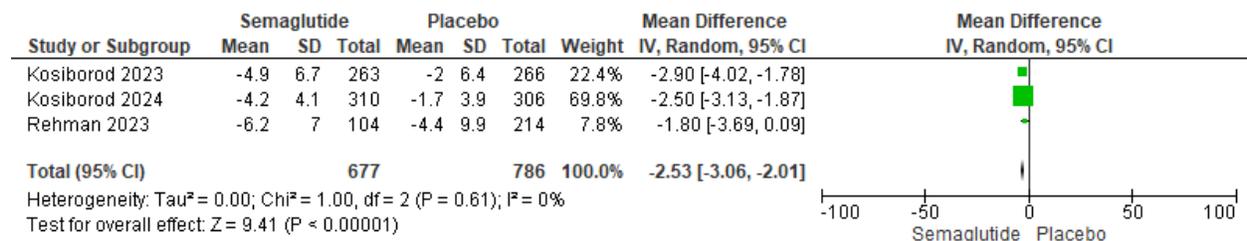
**Supplementary Figure 5:** Forest plot of Change in KCCQ-CSS from baseline to week 52



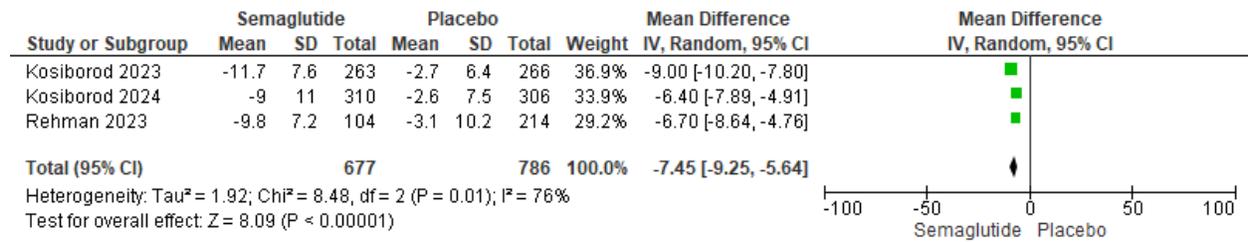
**Supplementary Figure 6:** Forest plot of Change from baseline to week 52 in KCCQ-OSS — points



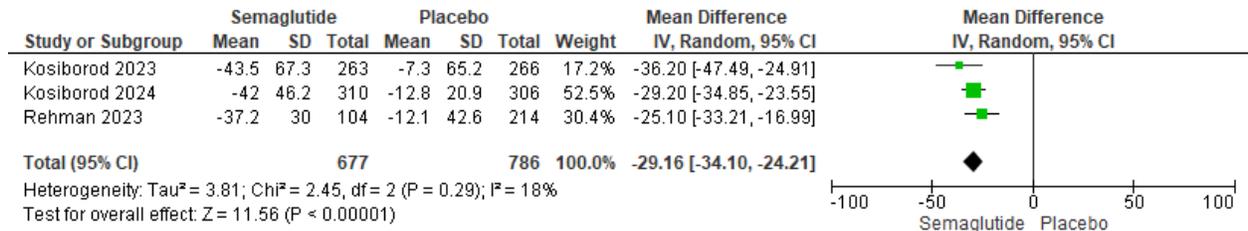
**Supplementary Figure 7:** Forest plot of Change from baseline to week 52 in systolic blood pressure — mm Hg



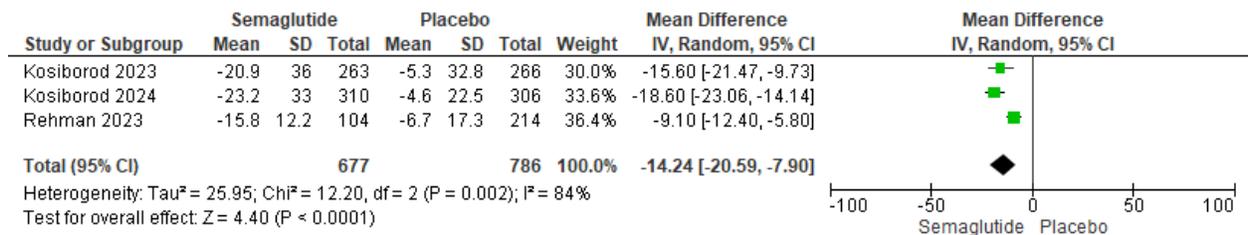
**Supplementary Figure 8:** Forest plot of Change from baseline to week 52 in waist circumference — cm



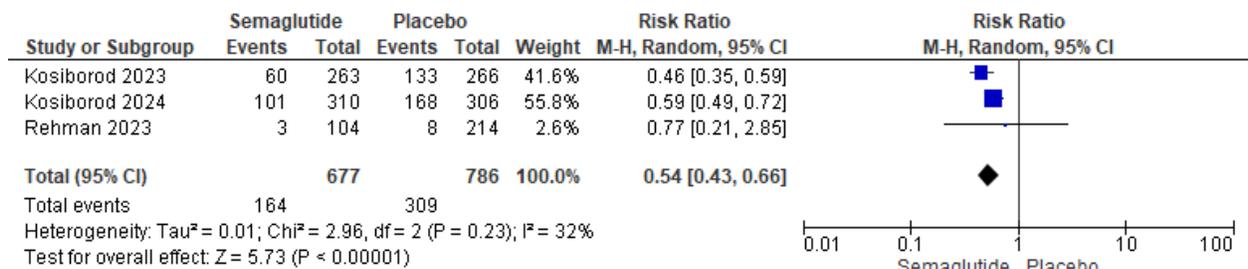
**Supplementary Figure 9:** Forest plot of 5 Change from baseline to week 52 in CRP level



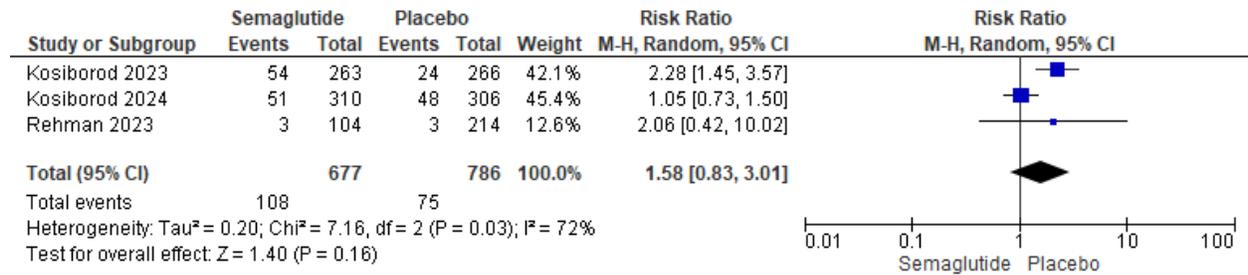
**Supplementary Figure 10:** Forest plot of 13 Change from baseline to week 52 in NT-proBNP level



**Supplementary Figure 11:** Forest plot of Serious adverse event



**Supplementary Figure 12:** Forest plot of Adverse events leading to permanent discontinuation of trial product, irrespective of seriousness



**Supplementary Figure 13:** Forest plot of Death from any cause

