

## Supplementary materials

**Table S1. Detailed search strategy.**

| Database                         | Search string                                                                                                                                                                                                                                                                |
|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PubMed MEDLINE<br>387 results    | ((("Cardiomyopathy, Hypertrophic"[Mesh]) OR (Hypertrophic Cardiomyopathies)) OR (Hypertrophic Obstructive Cardiomyopathies)) OR (Hypertrophic Obstructive Cardiomyopathy)) AND (((((Mavacamten) OR ("MYK-461")) OR (Aficamten)) OR (CK-274)) OR (Cardiac myosin inhibitors)) |
| ClinicalTrials.gov<br>31 results | Hypertrophic Cardiomyopathy   Aficamten OR Aficamten \ (CK-3773274\) \ (5 mg, 10 mg, 15 mg, and 20 mg\) OR Mavacamten OR cardiac myosin inhibitor OR MYK-461                                                                                                                 |
| Cochrane Library<br>114 results  | Cardiomyopathy, Hypertrophic MeSH AND cardiac myosin inhibitor OR Mavacamten OR MYK-461 OR Aficamten OR CK-274 OR CK-3773274                                                                                                                                                 |

MeSH: Medical Subject Headings.

**Table S2. PICO table, inclusion & exclusion criteria.**

|                     |                                                           |
|---------------------|-----------------------------------------------------------|
| <b>Patient</b>      | Hypertrophic cardiomyopathy                               |
| <b>Intervention</b> | Cardiac myosin inhibitors, either mavacamten or aficamten |
| <b>Comparator</b>   | Placebo drug                                              |

|                           |                                                                                                                                                                                                                                                                                                                                           |
|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Outcome</b>            | <p>Primary outcomes:</p> <ul style="list-style-type: none"> <li>• change in resting LVOT gradient</li> </ul> <p>Secondary outcomes:</p> <ul style="list-style-type: none"> <li>• proportion of patients achieving NYHA class improvement <math>\geq 1</math></li> <li>• change in left ventricular ejection fraction (LVEF)</li> </ul>    |
| <b>Study design</b>       | Randomized controlled trials                                                                                                                                                                                                                                                                                                              |
| <b>Inclusion criteria</b> | <ul style="list-style-type: none"> <li>• RCTs have patients with hypertrophic cardiomyopathy.</li> <li>• RCTs with patients being treated with Cardiac Myosin Inhibitors, either Mavacamten or Aficamten, compared with placebo</li> <li>• No restriction on race, age, gender, ethnicity, or publication date will be applied</li> </ul> |
| <b>Exclusion criteria</b> | <ul style="list-style-type: none"> <li>• Any observational study, case report, case series, conference paper</li> <li>• Patients not being treated with cardiac myosin inhibitors</li> <li>• Non-English language articles and non-randomized, one-arm studies</li> </ul>                                                                 |

LVOT: left ventricular outflow tract; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; RCTs: randomized controlled trials.

**Table S3. Datasheet for the decrease in resting LVOT gradient.**

| Author               | TE     | seTE   | treat1 | treat2 | treat1.long | treat.long | Versus    | Publication year |
|----------------------|--------|--------|--------|--------|-------------|------------|-----------|------------------|
| Olivotto et al. 2020 | -62.60 | 0.8608 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2020             |
| Desai et al. 2022    | -65.30 | 1.3315 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2022             |

|                   |        |        |    |    |            |         |           |      |
|-------------------|--------|--------|----|----|------------|---------|-----------|------|
| Tian et al.2023   | −57.83 | 8.2256 | MV | PL | Mavacamten | Placebo | MV vs. PL | 2023 |
| Maron et al. 2023 | −59.00 | 1.7183 | AF | PL | Aficamten  | Placebo | AF vs. PL | 2023 |
| Maron et al. 2024 | −29.63 | 5.3563 | AF | PL | Aficamten  | Placebo | AF vs. PL | 2024 |

LVOT: left ventricular outflow tract; TE: True Effect; seTE: standard error of True Effect; MV: mavacamten; PL: placebo; AF: aficamten. treat1 and treat2: these columns represent the first and second treatment groups, respectively; treat1.long and treat.long: these columns represent the full name of the abbreviations (treatment) used in the treat1 and treat2 columns, respectively.

**Table S4. Datasheet for NYHA class improvement.**

| Author               | TE     | seTE   | treat1 | treat2 | treat1.long | treat.long | Versus    | Publication year |
|----------------------|--------|--------|--------|--------|-------------|------------|-----------|------------------|
| Olivotto et al. 2020 | 2.0813 | 0.1468 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2020             |
| Ho et al. 2020       | 1.1536 | 0.3522 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2020             |
| Desai et al. 2022    | 2.9167 | 0.276  | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2022             |
| Tian et al.2023      | 4.000  | 0.4751 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2023             |
| Maron et al. 2023    | 1.7411 | 0.4517 | AF     | PL     | Aficamten   | Placebo    | AF vs. PL | 2023             |
| Maron et al. 2024    | 2.4068 | 0.1652 | AF     | PL     | Aficamten   | Placebo    | AF vs. PL | 2024             |

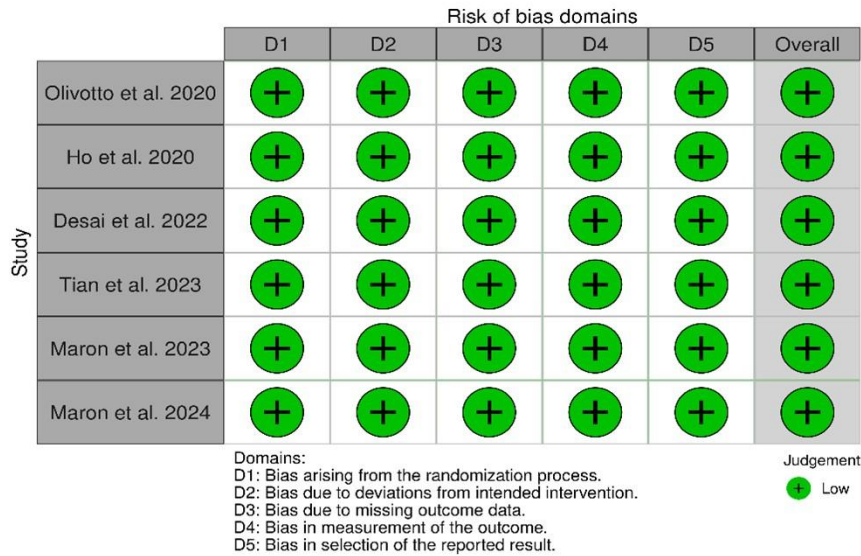
NYHA: New York Heart Association; TE: True Effect; seTE: standard error of True Effect; MV: mavacamten; PL: placebo; AF: aficamten. treat1 and treat2: these columns represent the first and

second treatment groups, respectively; treat1.long and treat.long: these columns represent the full name of the abbreviations (treatment) used in the treat1 and treat2 columns, respectively.

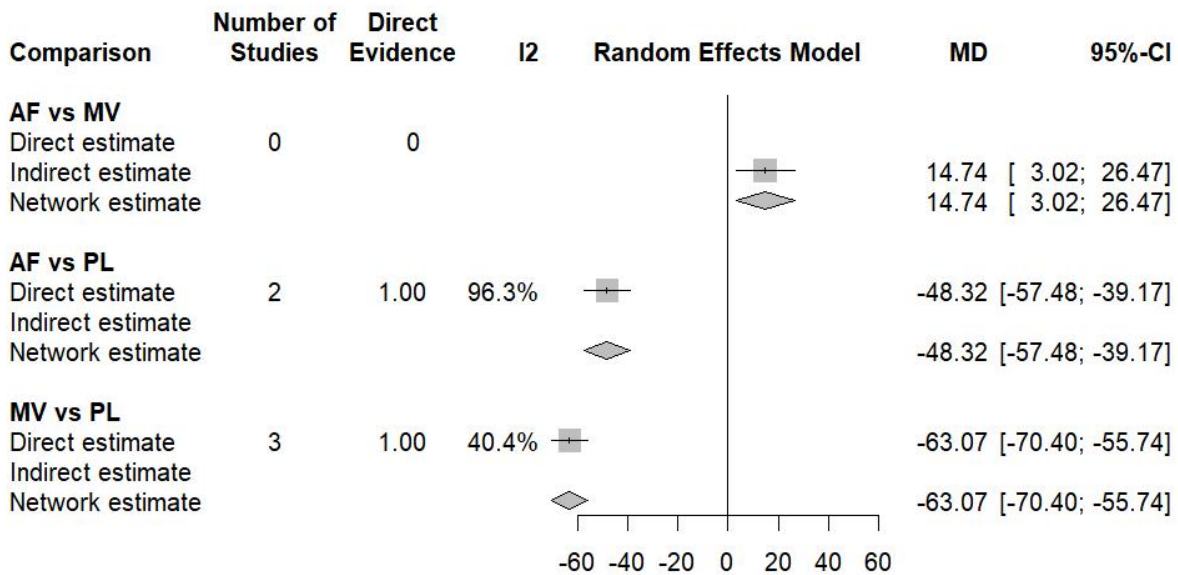
**Table S5. Datasheet for the decrease in LVEF.**

| Author               | TE    | seTE  | treat1 | treat2 | treat1.long | treat.long | Versus    | Publication year |
|----------------------|-------|-------|--------|--------|-------------|------------|-----------|------------------|
| Olivotto et al. 2020 | -5.2  | 0.036 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2020             |
| Ho et al. 2020       | -1.8  | 0.463 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2020             |
| Desai et al. 2022    | -4.0  | 0.765 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2022             |
| Tian et al. 2023     | 0.01  | 1.361 | MV     | PL     | Mavacamten  | Placebo    | MV vs. PL | 2023             |
| Maron et al. 2023    | -12.0 | 0.575 | AF     | PL     | Aficamten   | Placebo    | AF vs. PL | 2023             |
| Maron et al. 2024    | -4.8  | 0.791 | AF     | PL     | Aficamten   | Placebo    | AF vs. PL | 2024             |

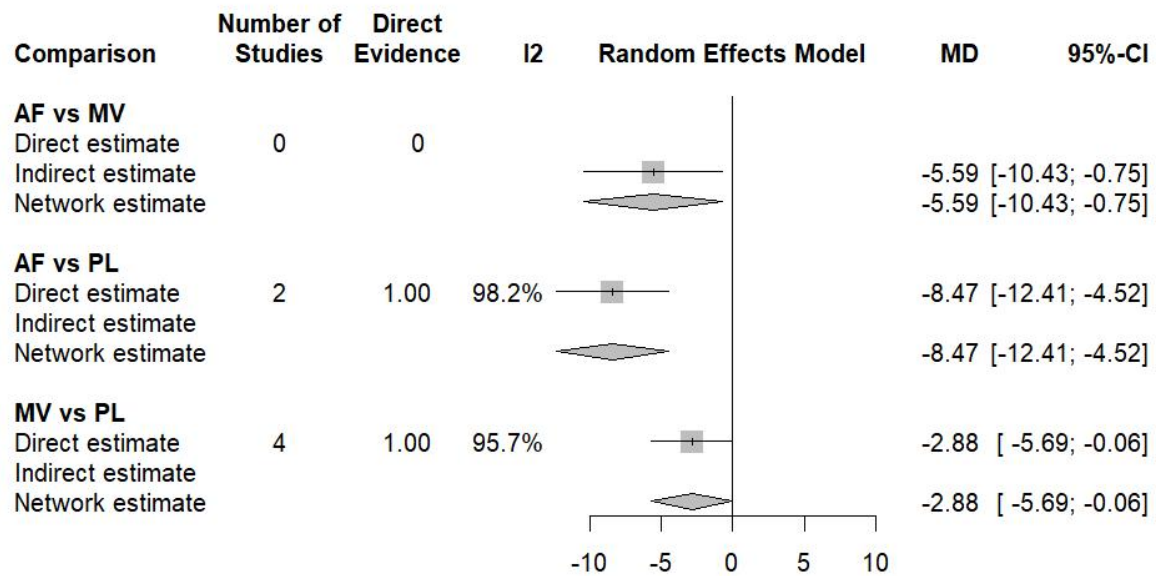
LVEF: left ventricular ejection fraction; TE: True Effect; seTE: standard error of True Effect; MV: mavacamten; PL: placebo; AF: aficamten. treat1 and treat2: these columns represent the first and second treatment groups, respectively; treat1.long and treat.long: these columns represent the full name of the abbreviations (treatment) used in the treat1 and treat2 columns, respectively.



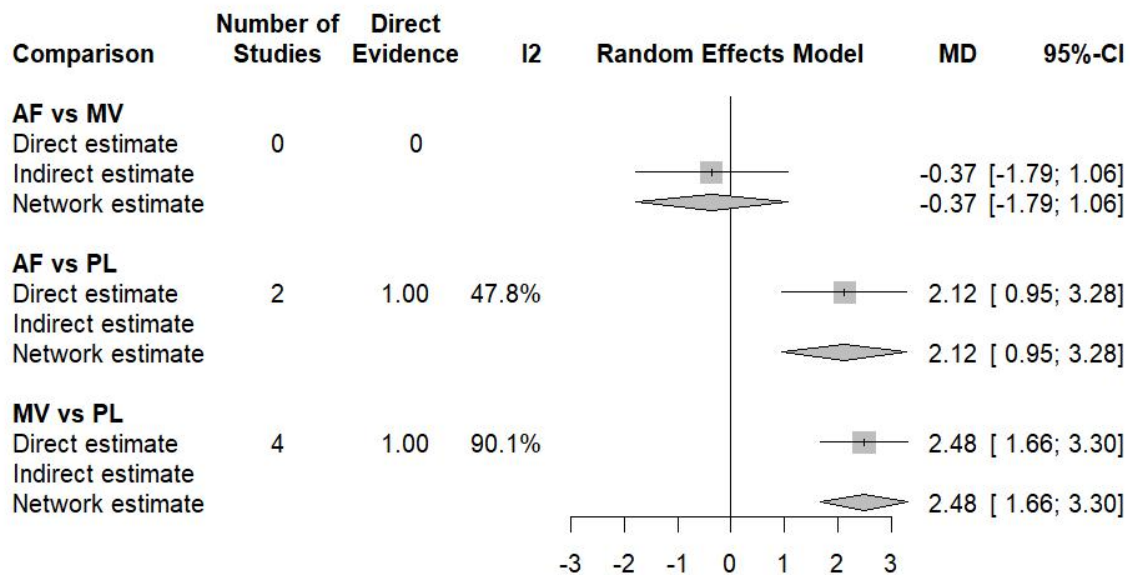
**Figure S1. Quality assessment of the included randomized controlled trials (RCTs).**



**Figure S2. Split network graph of the change in resting LVOT gradient. LVOT: left ventricular outflow tract; MD: mean difference.**



**Figure S3. Split network graph of change in LVEF.** LVEF: left ventricular ejection fraction; MD: mean difference.



**Figure S4. Split network graph of NYHA class improvement.** NYHA: New York Heart Association; MD: mean difference.