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## Supplemental Table 1. Details of included studies

| First Author (Year) | Single center or MC | n | Length of follow up, Days | Study design | Relevant Primary Outcome(s) | Risk of Bias | Quality of Evidence |
|---|---|---|---|---|---|---|---|
| **Full publication** | | | | | | | |
| Abraham, 2005 | MC (263) | 6247 | Duration of hospitalization | Prospective cohort study | In-hospital mortality; ICU and in-hospital LOS | No serious limitations | Moderate |
| Aranda, 2003 | Single center | 36 | Duration of hospitalization | Randomized controlled trial | In-hospital mortality; in-hospital LOS; symptomatic sustained or non-sustained arrhythmia requiring AAT | No Serious limitations | High |
| Arnold, 2006 | MC (32) | 1744 | 30 days following discharge | Retrospective cohort study | In-hospital mortality; in-hospital and ICU LOS; 30-day hospital readmission | Serious limitations | Moderate |
| Hauptman, 2008 | MC | 10 711 | Discharge from hospital or death | Retrospective cohort study | In-hospital mortality; in-hospital LOS | No serious limitations | Moderate |
| King, 2015 | Single center | 500 | 180 days following discharge or death | Retrospective cohort study | All-cause mortality; in-hospital LOS | Serious limitations | Moderate |
| Scroggins, 2005 | Single center | 67 | Discharge from hospital or death | Retrospective cohort study | In-hospital mortality; in-hospital and ICU LOS | Serious limitations | Moderate |
| Yamani, 2001 | Single center | 329 | Discharge from hospital or death | Retrospective cohort study | In-hospital mortality; arrhythmias (NSVT, sustained VT) | No serious limitations | Moderate |
| Lewis. 2019 | Single Center | 100 | Discharge from hospital or death | Retrospective cohort study | ICU or hospital LOS, in-hospital mortality | Serious limitations | Low |
| Gao, 2021 | Multicenter | 819 | All-cause hospital mortality | Retrospective cohort study | All-cause hospital mortality | Serious limitations | Low |
| Mathew, 2021 | Single center | 192 | In-hospital death from any cause | Randomized controlled trial | Discharge from hospital or death | No serious limitations | High |
| Nandekeolyar, 2021 | Single center | 326 | All-cause hospital mortality | Retrospective cohort study | Discharge from hospital or death | Serious limitations | Low |

AAT = anti-arrhythmia therapy; AMI = acute myocardial infarction; CRRT = continuous renal replacement therapy; LOS = length of stay; MC = multi-center

**Supplemental Table 2. Characteristics of patients treated with IV inotrope therapy in included studies**

| First Author (Year) | Age (years) | Indication for inotrope use | Mean dose (ug/kg/min) | LVEF | Known atrial arrhythmia prior to inotrope initiation |
|---|---|---|---|---|---|
| **Full publication** | | | | | |
| Abraham, 2005 | Dob 70.4<br>Mil 67.3 | ADHF | Dob 6.05<br>Mil 0.54 | LVEF ≤40% was<br>83% in Dob<br>89% in Mil groups | Dob 34%<br>Mil 33% |
| Aranda, 2003 | Dob 54<br>Mil 61 | ADHF with inotropic dependence | Dob 4.1<br>Mil 0.39 | Not provided | Not provided |
| Arnold, 2006 | Dob 63<br>Mil 61 | ADHF | | Not provided | Dob 31%<br>Mil 31% |
| Hauptman, 2008 | | AHDF | Not provided | Not provided | Not provided |
| King, 2015 | 63 (total)<br>Dob 63<br>Mil 62 | ADHF | Not provided | LVEF ≤40% was<br>48% (total)<br>Dob 47% and Mil 50% | Dob 16.3%<br>Mil 14.9% |
| Scroggins, 2005 | Not provided | ADHF | Not provided | Not provided | Not provided |
| Yamani, 2001 | Dob 61<br>Mil 62 | ADHF and NYHA class IV | Dob 5.8<br>Mil 0.5 | Dob LVEF of 17%<br>Mil LVEF of 18% | Dob 32%<br>Mil 28% |
| Lewis, 2019 | Dob 75<br>Mil 72.5 | Cardiogenic Shock | Not provided | Dob LVEF of 60%<br>Mil LVEF of 50% | Not provided |
| Gao, 2021 | Dob 67<br>Mil 65 | Cardiogenic Shock | Not provided | Not provided | Not provided |
| Mathew, 2021 | Dob 72<br>Mil 69 | Cardiogenic Shock | Not provided | Dob LVEF of 25%<br>Mil LVEF of 25% | Dob 46%<br>Mil 49% |
| Nandekeolyar, 2021 | Not provided | Cardiogenic Shock | Dob 3.7<br>Mil 0.27 | Not provided | Not provided |

ADHF = acute decompensated heart failure; IV = intravenous; LVF = Left ventricular failure; Dob = Dobutamine; Mil = Milrinone

## Supplemental Table 3. Definitions of clinically significant arrhythmias in included studies

| First Author (Year) | Definition of clinically significant arrhythmias provided in study |
|---|---|
| Aranda, 2003 | Ventricular arrhythmias requiring increased anti-arrhythmic therapy |
| Lewis, 2019 | Not provided [only reported as 'arrhythmia' including sinus tachycardia] |
| Yamani, 2001 | Non-sustained ventricular tachycardia [NSVT] and ventricular tachycardia [VT] |
| Mathew, 2021 | Arrhythmia leading to medical team intervention |

| **Supplemental Table 4. Medline Search Strategy (Update #2)**<br>*Database: MEDLINE(R) ALL 1946 to November 18, 2021*<br>*Platform: Ovid*<br>*Date Searched: November 19, 2021.* | |
|---|---|
| # | **Searches** |
| 1 | Milrinone/ |
| 2 | milrinon*.ti,ab,kf. |
| 3 | Phosphodiesterase 3 Inhibitors/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).ti,ab,kf. |
| 5 | win 47203.ti,ab,kf. |
| 6 | corotrop*.ti,ab,kf. |
| 7 | primacor.ti,ab,kf. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab,kf. |
| 10 | Dobutamine/ |
| 11 | Dobutamin*.ti,ab,kf. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | Animals/ |
| 15 | Humans/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to dt=20200701-20211119 |
| 19 | limit 17 to ed=20200701-20211119 |
| 20 | 18 or 19 |
| **Results: 40** | |

**Supplemental Table 5. Medline Search Strategy (Update #1)**
*Database: MEDLINE(R) ALL 1946 to July 02, 2020*
*Platform: Ovid*
*Date Searched: July 6, 2020*

| # | **Searches** |
|---|---|
| 1 | Milrinone/ |
| 2 | milrinon*.ti,ab,kf. |
| 3 | Phosphodiesterase 3 Inhibitors/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).ti,ab,kf. |
| 5 | win 47203.ti,ab,kf. |
| 6 | corotrop*.ti,ab,kf. |
| 7 | primacor.ti,ab,kf. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab,kf. |
| 10 | Dobutamine/ |
| 11 | Dobutamin*.ti,ab,kf. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | Animals/ |
| 15 | Humans/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to dt=20161201-20200706 |
| 19 | limit 17 to ed=20161201-20200706 |
| 20 | 18 or 19 |
| **Results: 65** | |

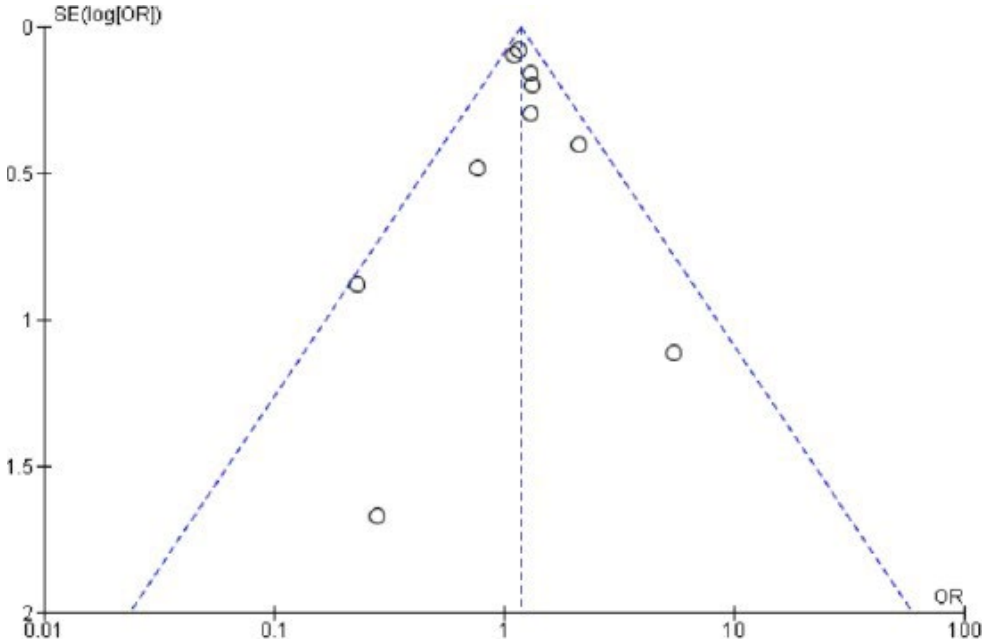
| **Supplemental Table 6. CENTRAL Search Strategy (Update #2)**<br>*Database: EBM Reviews - Cochrane Central Register of Controlled Trials October 2021*<br>*Platform: Ovid*<br>*Date Searched: November 19, 2021* | |
|---|---|
| # | **Searches** |
| 1 | Milrinone/ |
| 2 | milrinon*.ti,ab. |
| 3 | Phosphodiesterase 3 Inhibitors/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).ti,ab. |
| 5 | win 47203.ti,ab. |
| 6 | corotrop*.ti,ab. |
| 7 | primacor.ti,ab. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab. |
| 10 | Dobutamine/ |
| 11 | Dobutamin*.ti,ab. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | Animals/ |
| 15 | Humans/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to yr="2020 -Current" |
| **Results: 8** | |

| **Supplemental Table 7. CENTRAL Search Strategy (Update #1)**<br>*Database: EBM Reviews - Cochrane Central Register of Controlled Trials May 2020*<br>*Platform: Ovid*<br>*Date Searched: July 6, 2020* | |
|---|---|
| # | **Searches** |
| 1 | Milrinone/ |
| 2 | milrinon*.ti,ab,kw. |
| 3 | Phosphodiesterase 3 Inhibitors/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).ti,ab,kw. |
| 5 | win 47203.ti,ab,kw. |
| 6 | corotrop*.ti,ab,kw. |
| 7 | primacor.ti,ab,kw. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab,kw. |
| 10 | Dobutamine/ |
| 11 | Dobutamin*.ti,ab,kw. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | Animals/ |
| 15 | Humans/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to yr="2016 -Current" |
| **Results: 28** | |

| **Supplemental Table 8. Embase Search Strategy (Update #2)**<br>*Database: Embase Classic+Embase 1947 to 2021 November 18*<br>*Platform: Ovid*<br>*Date Searched: November 19, 2021* | |
|---|---|
| # | **Searches** |
| 1 | milrinone/ |
| 2 | milrinon*.ti,ab,kw. |
| 3 | phosphodiesterase III inhibitor/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).ti,ab,kw. |
| 5 | win 47203.ti,ab,kw. |
| 6 | corotrop*.ti,ab,kw. |
| 7 | primacor.ti,ab,kw. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab,kw. |
| 10 | exp dobutamine/ |
| 11 | Dobutamin*.ti,ab,kw. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | animal/ |
| 15 | human/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to dd=20200701-20211119 |
| 19 | limit 17 to dc=20200701-20211119 |
| 20 | 18 or 19 |
| **Results: 264** | |

| **Supplemental Table 9. Embase Search Strategy (Update #1)**<br>*Database: Embase Classic+Embase 1947 to 2020 July 02*<br>*Platform: Ovid*<br>*Date Searched: July 6, 2020* | |
|---|---|
| # | **Searches** |
| 1 | milrinone/ |
| 2 | milrinon*.tw. |
| 3 | phosphodiesterase III inhibitor/ |
| 4 | (Phosphodiesterase adj3 inhibitor*).tw. |
| 5 | win 47203.tw. |
| 6 | corotrop*.tw. |
| 7 | primacor.tw. |
| 8 | 1 or 2 or 3 or 4 or 5 or 6 or 7 |
| 9 | Dobutrex.ti,ab,kw. |
| 10 | exp dobutamine/ |
| 11 | Dobutamin*.ti,ab,kw. |
| 12 | 9 or 10 or 11 |
| 13 | 8 and 12 |
| 14 | animal/ |
| 15 | human/ |
| 16 | 14 not 15 |
| 17 | 13 not 16 |
| 18 | limit 17 to dd=20161201-20200706 |
| 19 | limit 17 to dc=20161201-20200706 |
| 20 | 18 or 19 |
| **Results: 517** | |

**Supplemental Figure 1: Funnel plot of comparison of In-Hospital Mortality**



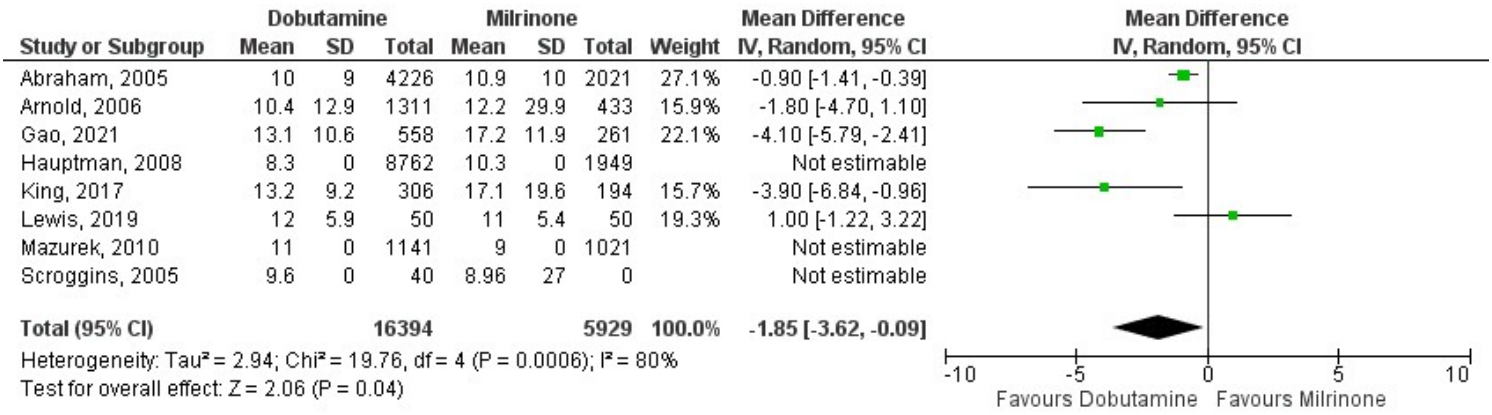
## Supplemental Figure 2: PRISMA Checklist

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | Page 2, Paragraph 2 |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Page 1 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Page 1, Paragraph 1 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Page 1, Paragraph 2 |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Page 3, Paragraph 2 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 2, Paragraph 5 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Supplemental Table 4,5,6 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Page 3, Paragraph 3 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 3, Paragraph 3 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page 2, Paragraph 4 |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 2, Paragraph 4 |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 3, Paragraph 3 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Page 3, Paragraph 5 |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Page 3, Paragraph 5 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Page 3, Paragraph 5 |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Figure 2, 3, 4, 5 |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software | Page 3, Paragraph 5 |

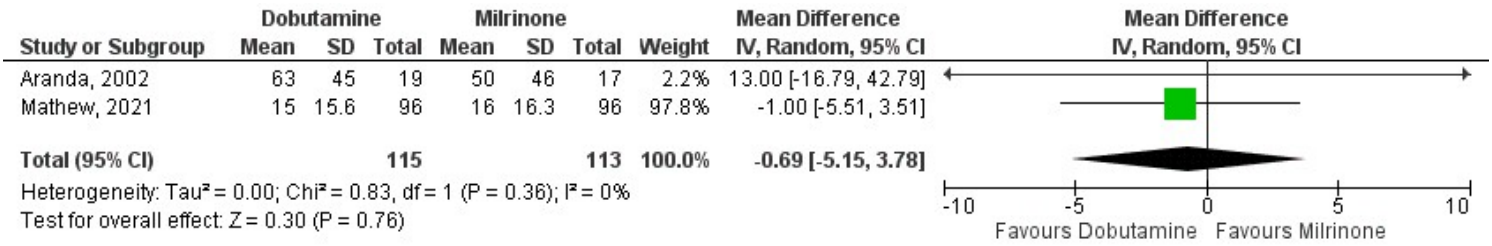
| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | package(s) used. | |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Page 3, Paragraph 5 |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Page 5, Paragraph 2 |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Page 3, Paragraph 4 |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Page 3, Paragraph 5 |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Page 4, Paragraph 1 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Page 4, Paragraph 1 |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Page 4, Paragraph 3, 5, 6, 7. Supplemental Table 1 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supplemental Table 1 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Figures 2-5 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Supplemental Table 1 |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Figures 2-5 |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Supplemental Figure 1 |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Supplemental Figure 2 |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Supplemental Table 1 |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Supplemental table 1 |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Page 5, Paragraph 5 |
| | 23b | Discuss any limitations of the evidence included in the review. | Page 6, Paragraph 4 |
| | 23c | Discuss any limitations of the review processes used. | Page 6, Paragraph 4 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Page 6 Paragraph 3 |
| **OTHER INFORMATION** | | | |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | Page 2, Paragraph 3 |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Page 2, paragraph 3 |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | Page 2, paragraph 4 |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | n/a, cover letter |
| Competing interests | 26 | Declare any competing interests of review authors. | n/a, cover letter |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 2, paragraph 3 |

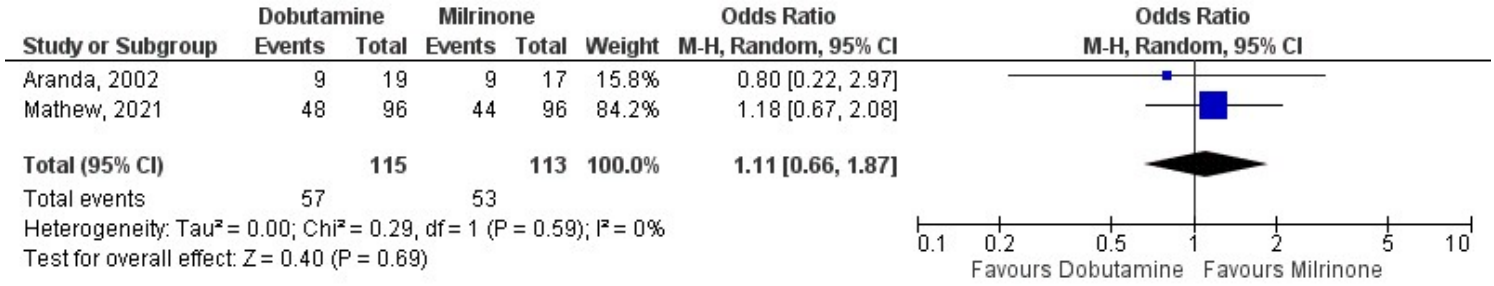
**Supplemental Figure 3: Forest plot of in-hospital LOS with dobutamine versus milrinone inotrope therapy (observational studies).**



**Supplemental Figure 4: Forest plot of in-hospital LOS with dobutamine versus milrinone inotrope therapy (randomized studies).**



**Supplemental Figure 5: Forest plot of arrhythmias with dobutamine versus milrinone inotrope therapy (observational studies).**



**Supplemental Figure 6: Forest plot of arrhythmias with dobutamine versus milrinone inotrope therapy (randomized studies).**