**Supplemental Appendix - Table of Contents**

Alberta SPOR SUPPORT Unit | Knowledge Translation Platform

**Search Log for: COVID-19/ARDS and Shunts**

FINALIZED: 26 Mar 2021

**Electronic Databases Searches**

| Import # | Database Name* | Search Interface | Database Dates | Date of Search MM/DD/YYYY | Initial Count | Post De-dupe |
|---|---|---|---|---|---|---|
| 1 | Medline | Ovid | 1946 to Present | 03/24/2021 | 1190 | 1187 |
| 2 | Embase | Ovid | 1974 to Present | 03/24/2021 | 3314 | 2381 |
| 3 | Cochrane | Wiley | Inception – Present | 03/24/2021 | 90 | 22 |
| 4 | DARE | NHS | Inception - Present | 03/24/2021 | 23 | 23 |
| | | | | **Total Database Search Results**: | **4617** | **3613*** |

**Location of search result folder and file names: Z:\KS Projects\Lau - ARDS Shunts**

**Librarian(s)/researcher(s) conducting search strategy** ((initials) name, degree(s))**:**
(DKL) Diana Keto-Lambert, MLIS; Peer review by Doug Salzwedel, MLIS

Appendix: Search Strategies
Database(s): **Ovid MEDLINE(R) ALL** 1946 to March 26, 2021
Search Title: ARDS-Shunts_1
Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | exp respiratory insufficiency/ | 63943 |
| 2 | Respiratory distress syndrome/ | 20797 |
| 3 | (respiratory adj2 insufficien*).tw,kf. | 9354 |
| 4 | (respiratory adj2 fail*).tw,kf. | 34680 |
| 5 | (respiratory adj2 distress*).tw,kf. | 44807 |
| 6 | ARDS*.tw,kf. | 14634 |
| 7 | AHRF*.tw,kf. | 195 |
| 8 | (CARDS or C-ARDS).tw,kf. | 10669 |
| 9 | COVID-19/ | 66643 |
| 10 | Coronavirus Infections/ | 44654 |
| 11 | Coronavirus/ | 4572 |
| 12 | Betacoronavirus/ | 33199 |
| 13 | SARS-CoV-2/ | 51893 |
| 14 | Covid*.tw,kf. | 104925 |
| 15 | (nCov or novel-CoV or 2019nCoV).tw,kf. | 1790 |
| 16 | (CoV-2 or CoV2 or sarscov2 or sarscov-2).tw,kf. | 38362 |
| 17 | Wuhan-virus*.tw,kf. | 18 |
| 18 | ((wuhan or hubei or huanan) and (severe-acute-respiratory or pneumonia*) and outbreak*).tw,kf. | 976 |
| 19 | or/1-18 [ARDS/COVID] | 266102 |

| | | |
|---|---|---|
| 20 | Echocardiography, Transesophageal/ | 21268 |
| 21 | transpulmonary bubble.tw,kf. | 4 |
| 22 | agitated saline.tw,kf. | 350 |
| 23 | ((bubble or microbubble) adj3 (study or studies)).tw,kf. | 441 |
| 24 | (bubble adj3 echocardiogra*).tw,kf. | 125 |
| 25 | (Saline contrast adj3 (study or studies)).tw,kf. | 30 |
| 26 | TPBT*.tw,kf. | 8 |
| 27 | transthoracic echocardiogra*.tw,kf. | 14148 |
| 28 | ((transesophageal or transoesophageal) adj2 echocardiogra*).tw,kf. | 18799 |
| 29 | (vascular adj2 dilat*).tw,kf. | 1603 |
| 30 | ((intracardiac* or intra-cardiac* or cardiac*) adj3 shunt*).tw,kf. | 1727 |
| 31 | ((intrapulmonary* or intra-pulmonary* or pulmonary*) adj3 shunt*).tw,kf. | 4250 |
| 32 | or/20-31 [DIAGNOSING SHUNTS] | 47784 |
| 33 | 19 and 32 | 1190 |

Database(s): **Embase** 1974 to 2021 March 23
Search Title: ARDS-Shunts_2
Search Strategy:

| # | Searches | Results |
|---|---|---|
| 1 | exp respiratory failure/ | 104935 |
| 2 | Respiratory distress syndrome/ | 14477 |
| 3 | Adult respiratory distress syndrome/ | 42416 |
| 4 | (respiratory adj2 insufficien*).tw,kw. | 11103 |
| 5 | (respiratory adj2 fail*).tw,kw. | 59497 |
| 6 | (respiratory adj2 distress*).tw,kw. | 65370 |
| 7 | ARDS*.tw,kw. | 24438 |
| 8 | AHRF*.tw,kw. | 387 |
| 9 | (CARDS or C-ARDS).tw,kw. | 15465 |
| 10 | exp Coronavirinae/ | 23440 |
| 11 | Coronavirus Infection/ | 13028 |
| 12 | SARS coronavirus/ | 6308 |
| 13 | Covid*.tw,kw. | 105002 |
| 14 | (nCov or novel-CoV or 2019nCoV).tw,kw. | 1823 |
| 15 | (CoV-2 or CoV2 or sarscov2 or sarscov-2).tw,kw. | 37348 |
| 16 | Wuhan-virus*.tw,kw. | 13 |
| 17 | ((wuhan or hubei or huanan) and (severe-acute-respiratory or pneumonia*) and outbreak*).tw,kw. | 1047 |
| 18 | or/1-17 [ARDS/COVID] | 336353 |
| 19 | Transesophageal echocardiography/ | 47413 |
| 20 | Contrast echocardiography/ | 4108 |
| 21 | Heart septum defect/ | 7685 |
| 22 | Pulmonary shunt/ | 1293 |
| 23 | transpulmonary bubble.tw,kw. | 5 |
| 24 | agitated saline.tw,kw. | 788 |

| | | |
|---|---|---|
| 25 | ((bubble or microbubble) adj3 (study or studies)).tw,kw. | 866 |
| 26 | (bubble adj3 echocardiogra*).tw,kw. | 374 |
| 27 | (Saline contrast adj3 (study or studies)).tw,kw. | 61 |
| 28 | TPBT*.tw,kw. | 9 |
| 29 | transthoracic echocardiogra*.tw,kw. | 29407 |
| 30 | ((transesophageal or transoesophageal) adj2 echocardiogra*).tw,kw. | 28375 |
| 31 | (vascular adj2 dilat*).tw,kw. | 2316 |
| 32 | ((intracardiac* or intra-cardiac* or cardiac*) adj3 shunt*).tw,kw. | 2658 |
| 33 | ((intrapulmonary* or intra-pulmonary* or pulmonary*) adj3 shunt*).tw,kw. | 6029 |
| 34 | or/19-33 [DIAGNOSING SHUNTS] | 97883 |
| 35 | 18 and 34 | 3314 |

Database: Cochrane Library (Cochrane Reviews & Trials)
Search Name: ARDS-Shunts_3
Date Run: 25/03/2021 10:21:08
Comment:

| ID | Search | Hits |
|---|---|---|
| #1 | [mh "respiratory insufficiency"] | 2854 |
| #2 | [mh ^"Respiratory distress syndrome"] | 1392 |
| #3 | (respiratory near/2 insufficien*):ti,ab,kw | 2009 |
| #4 | (respiratory near/2 fail*):ti,ab,kw | 4889 |
| #5 | (respiratory near/2 distress*):ti,ab,kw | 6814 |
| #6 | ARDS*:ti,ab,kw | 2034 |
| #7 | AHRF*:ti,ab,kw | 86 |
| #8 | (CARDS or C-ARDS):ti,ab,kw | 2260 |
| #9 | [mh ^"Covid-19"] | 257 |
| #10 | [mh ^"Coronavirus infections"] | 596 |
| #11 | [mh ^Coronavirus] | 3 |
| #12 | [mh ^Betacoronavirus] | 128 |
| #13 | [mh ^"SARS-CoV-2"] | 204 |
| #14 | Covid*:ti,ab,kw | 4497 |
| #15 | (nCov or "novel COV" or 2019nCoV):ti,ab,kw | 141 |
| #16 | ("COV-2" or COV2 or sarscov2 or "sarscov-2"):ti,ab,kw | 1742 |
| #17 | "wuhan virus*":ti,ab,kw | 0 |
| #18 | ((wuhan or hubei or huanan) and ("severe acute respiratory" or pneumonia*) and outbreak*):ti,ab,kw | 40 |
| #19 | {or #1-#18} | 19342 |
| #20 | [mh ^"Echocardiography, transesophageal"] | 418 |
| #21 | "transpulmonary bubble":ti,ab,kw | 0 |
| #22 | "agitated saline":ti,ab,kw | 26 |
| #23 | ((bubble or microbubble) near/3 (study or studies)):ti,ab,kw | 38 |
| #24 | (bubble near/3 echocardiogra*):ti,ab,kw | 2 |
| #25 | ("saline contrast" near/3 (study or studies)):ti,ab,kw | 1 |
| #26 | TPBT*:ti,ab,kw | 0 |
| #27 | "transthoracic echocardiogra*":ti,ab,kw | 0 |
| #28 | ((transesophageal or transoesophageal) near/2 echocardiogra*):ti,ab,kw | 1101 |
| #29 | (vascular near/2 dilat*):ti,ab,kw | 79 |
| #30 | ((intracardiac* or "intra cardiac*" or cardiac*) near/3 shunt*):ti,ab,kw | 66 |
| #31 | ((intrapulmonary* or "intra pulmonary*" or pulmonary*) near/3 shunt*):ti,ab,kw | 450 |
| #32 | {or #20-#31} | 1720 |
| #33 | #19 and #32 | 90 (Only trials; no Cochrane reviews were available) |

Database: DARE (Database of Abstracts for Reviews or Effects)
Search Strategy:
Results for: (respiratory insufficien* or respiratory fail* or respiratory distress* or ARDS* or AHRF* or CARDS or COVID* or SARS* or COV2* or COV-2* or nCov or novel cov* or corona* or pneumonia* outbreak* or severe acute respiratory) AND (transesophageal echocardiograp* or transoesophageal echocardiograp* or transthoracic echocardiograp* or transpulmonary bubble or agitated saline or bubble study or bubble studies or bubble echocardiograp* or saline contrast or TPBT* or vascular dilat* or shunt*) 23
Note: No filters were available to translate from DARE to EndNote, so they were entered by hand.
*An additional 5 duplicates were removed by Covidence for a total of 3608

**Supplements**:
Supplemental Table 1: PRISMA Checklist

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 3 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 3 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3,4 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3,4 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 3,4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 3,4 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 3,4 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 4 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 4 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | 4 |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 4 |
| **RESULTS** | | | |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 4-5 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 4-5 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | 4-5 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 4-5 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 4-5 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 4-5 |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 4-5 |
| **DISCUSSION** | | | |
| Summary of evidence | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 6-7 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 6-7 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 6-7 |
| **FUNDING** | | | |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | N/A |

*From:* Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097
For more information, visit: **www.prisma-statement.org**.

Supplemental Table 2: Risk of Bias Joanne Briggs Institute

| | Were the 2 groups similar and recruited from the same population? | Were the exposures measured similarly to assign people to both exposed and unexposed groups? | Was the exposure measured in a valid and reliable way? | Were the confounding factors identified? | Were strategies to deal with confounding factors stated? | Were the groups / participants free of the outcome at the start of the study (or at the moment of exposure)? | Were the outcome measured in a valid and reliable way? | Was the follow-up time reported sufficient to be long enough for outcome to occur? | Was follow up complete, and if not, were the reasons to loss to follow up described and explored? | Were strategies to address incomplete follow-up utilized? | Was appropriate statistical analysis used? | Overall appraisal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Observational cohort (9)** | | | | | | | | | | | | |
| Boissier 2015 | Yes | Yes | Yes | Yes | Unclear | Yes | Yes | Unclear | Yes | Unclear | Yes | Include |
| Legras 2015 | Yes | Yes | Yes | Unclear | Unclear | Yes | Yes | Yes | Yes | Unclear | Yes | Include |
| Lhertier 2013 | Yes | Yes | Yes | Unclear | Unclear | Yes | Yes | Yes | Yes | Yes | Yes | Include |
| Masi 2020 | NA | No | Unclear | No | No | Unclear | No | NA | NA | Unclear | NA | Exclude |
| Mekontso Dessap 2010 | Yes | Yes | Yes | Unclear | No | Yes | Yes | Yes | Yes | Unclear | Yes | Include |
| Mekontso Dessap 2011 | NA | No | Unclear | No | Unclear | Unclear | No | NA | NA | Unclear | NA | Exclude |
| Salazar-Orellana 2021 | Yes | Yes | Yes | Yes | Unclear | Yes | Yes | Unclear | Unclear | Unclear | Yes | Include |
| Vavlitou 2010 | Yes | Yes | Yes | Unclear | Unclear | Yes | No | NA | NA | Unclear | NA | Exclude |
| Vedrienne 1995 | Unclear | Yes | Yes | No | No | Unclear | Unclear | Yes | Yes | Unclear | Yes | Include |
| **Cross-sectional pilot study (1)** | | | | | | | | | | | | |
| Reynolds 2020 | NA | No | Unclear | Unclear | No | Unclear | No | NA | NA | Unclear | NA | Exclude |

Supplemental Table 3: Risk of Bias Newcastle-Ottawa Scale

| | Representativeness of exposed cohort (/1) | Representativeness of non-exposed cohort (/1) | Ascertainment of exposure (/1) | Demonstration outcome of interest not present at initiation of study (/1) | Comparability of cohorts (/2) | Assessment of outcome (/1) | Was follow-up long enough for outcome to occur? (/1) | Was follow-up adequate? (/1) | Total score (/9) | Overall Risk of Bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Observational cohort (9) | | | | | | | | | | |
| Boissier 2015 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | **7** | **Poor** |
| Legras 2015 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | **8** | **Good** |
| Lhertier 2013 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | **8** | **Good** |
| Masi 2020 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | **4** | **Poor** |
| Mekontso Dessap 2010 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | **8** | **Good** |
| Mekontso Dessap 2011 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | **5** | **Poor** |
| Salazar-Orellana 2021 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 1 | **7** | **Good** |
| Vavlitou 2010 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | **5** | **Poor** |
| Vedrienne 1995 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | **6** | **Fair** |
| Cross-sectional pilot study (1) | | | | | | | | | | |
| Reynolds 2020 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | **5** | **Poor** |

Supplemental Table 4: Grading of Recommendations Assessment, Development and Evaluation (GRADE) of ARDS Shunt Outcomes: mortality, oxygenation

| Certainty assessment | | | | | | | | | | | Impact | Certainty | Importance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| № of studies | Study design (sources, n) | Anticipated absolute effects [95% CI]* Risk with shunt (n, %) | Anticipated absolute effects [95% CI]* Risk without shunt (n, %) | Relative effect [95% CI]* | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication Bias | Other considerations (e.g. large magnitude of effect, addressed residual confounding) | | | |
| Outcome: Mortality | | | | | | | | | | | | | |
| 5 | Observational studies (5 cohort)<br><br>(n = 845) | 69/163 (42.3%)<br><br>[95% CI: 34.6-50.3] | 218/682 (32.0%)<br><br>[95% CI: 28.5-35.6] | Shunt presence:<br><br>RR 1.22 [95% CI: 1.01 to 1.49]<br>p = 0.04 | serious [a] | not serious [b] | not serious [c] | not serious [d] | undetected [f] | none [g] | - *Mortality data was limited to 5 observational studies that included comparators of shunt and non-shunt groups.*<br>- *No individual study reported a statistically significant difference in mortality between shunt and non-shunt groups. However, during meta-analysis, pooling of data resulted in a statistically significant result (RR 1.22 [95% CI 1.01-1.49]).*<br>- *Given all observational studies start at a "low certainty rating", plus downgrades for RoB,would consider the certainty in the evidence to be "very low" quality for mortality* | ⨁◯◯◯Very Low Quality | CRITICAL |
| № of studies | Study design (sources, n) | Anticipated absolute effects Risk without shunt (mean ± SD) | Anticipated absolute effects Risk without shunt (mean ± SD) | Relative effect [95% CI]* | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication Bias | Other considerations (e.g. large magnitude of effect, addressed residual confounding) | Impact | Certainty | Importance |
| Outcome: Oxygenation (P:F ratio, $P_aO_2$ / $FiO_2$) | | | | | | | | | | | | | |
| 5 | Observational studies (5 cohort)<br><br>(n = 700) | 123.8 ± 51.0 | 124.5 ± 46.3 | Shunt presence:<br><br>Mean difference: PF ratio: -0.7 [95% CI: -18.6 to 17.2]<br>p =0.94) | serious [a] | very serious [b] | not serious [c] | serious [d] | undetected [f] | none [g] | - *Oxygenation data was limited to 5 observational studies that included comparators of shunt and non-shunt groups.*<br>- *Individual studies demonstrated very serious inconsistency with significant variance in study population, shunt assessment modality and overall impact on oxygenation. This is reflectedin oxygenation outcome data with studies demonstrating differences between groups favoring both shunt and non-shunt groups amongst included studies (n=5)*<br>- *Given all observational studies start at a "low certainty rating", plus downgrades for RoB, inconsistency and imprecision, would consider the certainty in the evidence to be "very low" quality for oxygenation* | ⨁◯◯◯Very Low Quality | MODERATE |

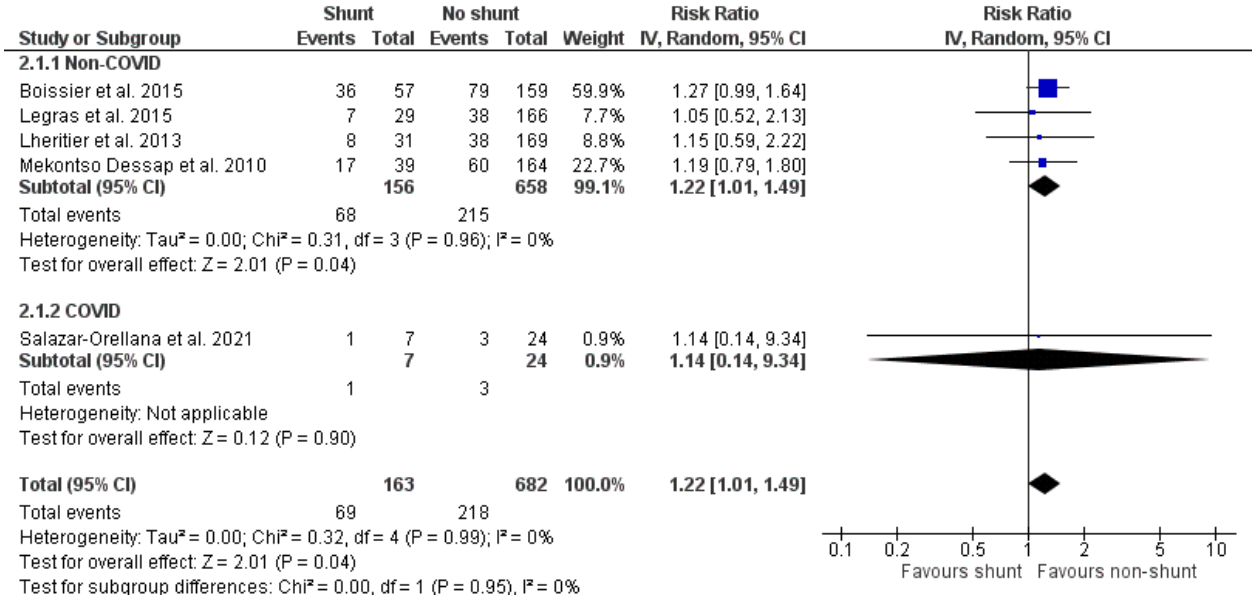
CI: Confidence interval, DDH: direct discharge home, DISH: Direct from ICU Sent Home, ED: emergency department, GRADE: Grading of Recommendations Assessment, Development and Evaluation, ICU: intensive care unit, IV: instrumental variable, JBI: Joanna Briggs Institute, n: number; NOS: Newcastle-Ottawa Scale, RCT: randomized control trial, RR: relative risk; SD: standard deviation

** The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparator group and the relative effects of the intervention group (and its 95% CI)*

a. Risk of bias rating of "serious" based on fair score (using NOS RoB tool) in 10% (1/10) of studies and good score (using NOS ROB tool) in only 40% (4/10) of studies.
b. Inconsistency rating based on $I^2$ of studies with "not serious" <50%, "serious" 51-75% and "very serious">75%.
c. Indirectness rating of "not serious" given all included studies measured the same direct quantitative assessment of mortality and oxygenation (by P:F ratio)
d. Imprecision rating of "not serious" given for mortality as 95% confidence interval for composite meta-analysis data did not cross 1.00 RR and "serious" for oxygenation where CIs were very wide and crossed 1.00 RR.
e. No additional significant other considerations including publication bias, unidentified studies or statistical error were felt to significantly impact the summary of findings
f. No publication bias detected (although cannot be ruled out); could potentially be present for mortality
g. No other considerations for upgrading

**Supplemental Figures**

Supplemental Figure 1: Subgroup analyses of COVID vs. non-COVID studies (Forest plot for mortality in ARDS shunt)



Supplemental Figure 2: Subgroup analyses of COVID vs. non-COVID studies (Forest plot for oxygenation in ARDS shunt)

| Study or Subgroup | Shunt Mean | SD | Total | No Shunt Mean | SD | Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| **3.1.1 Non-COVID** | | | | | | | | |
| Boissier et al. 2015 | 125 | 56 | 57 | 120 | 56 | 159 | 21.5% | 5.00 [-11.94, 21.94] |
| Lheritier et al. 2013 | 106 | 40 | 31 | 116 | 39 | 169 | 22.3% | -10.00 [-25.26, 5.26] |
| Mekontso Dessap et al. 2010 | 122 | 58 | 39 | 114 | 45 | 165 | 20.3% | 8.00 [-11.45, 27.45] |
| Vedrinne et al. 1995 | 120 | 17 | 11 | 145 | 10 | 38 | 24.4% | -25.00 [-35.54, -14.46] |
| **Subtotal (95% CI)** | | | **138** | | | **531** | **88.5%** | **-6.70 [-22.95, 9.56]** |
| Heterogeneity: Tau² = 211.83; Chi² = 13.84, df = 3 (P = 0.003); I² = 78% | | | | | | | | |
| Test for overall effect: Z = 0.81 (P = 0.42) | | | | | | | | |
| **3.1.2 COVID** | | | | | | | | |
| Salazar-Orellana et al. 2021 | 251 | 41 | 7 | 208 | 64 | 24 | 11.5% | 43.00 [3.27, 82.73] |
| **Subtotal (95% CI)** | | | **7** | | | **24** | **11.5%** | **43.00 [3.27, 82.73]** |
| Heterogeneity: Not applicable | | | | | | | | |
| Test for overall effect: Z = 2.12 (P = 0.03) | | | | | | | | |
| **Total (95% CI)** | | | **145** | | | **555** | **100.0%** | **-0.69 [-18.56, 17.18]** |
| Heterogeneity: Tau² = 311.86; Chi² = 20.92, df = 4 (P = 0.0003); I² = 81% | | | | | | | | |
| Test for overall effect: Z = 0.08 (P = 0.94) | | | | | | | | |
| Test for subgroup differences: Chi² = 5.15, df = 1 (P = 0.02), I² = 80.6% | | | | | | | | |