# Unexplained mortality differences between septic shock trials: A systematic analysis of population characteristics and control-group mortality rates.

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**ELECTRONIC SUPPLEMENTARY MATERIAL – ADDITIONAL METHODS AND RESULTS**

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**1. PRISMA checklist**

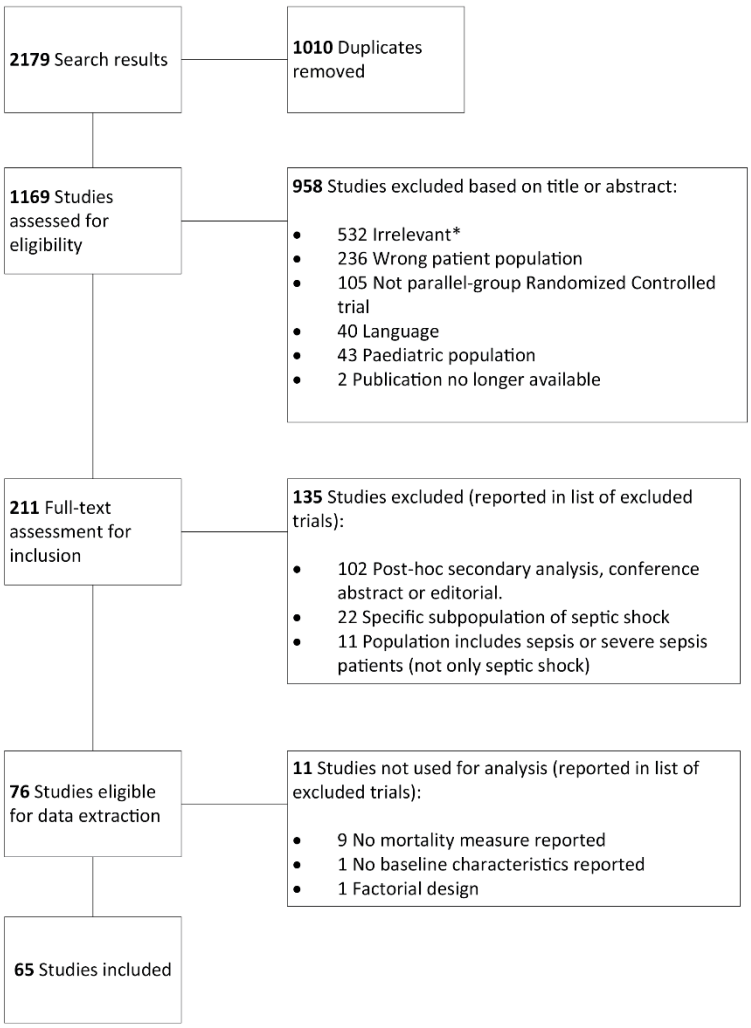
| Section/topic | # | Checklist item | Reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | Yes |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; 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. | Yes |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | Yes |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Yes |
| **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. | Yes |
| 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. | Yes |
| 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. | Yes |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Yes |
| 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). | Yes |
| 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. | Yes |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Yes |
| 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. | Not applicable |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | Yes |
| 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. | Yes |

| Section/topic | # | Checklist item | Reported |
|---|---|---|---|
| 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). | Not applicable |
| Additional analyses | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | Yes |
| **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. | Yes |
| 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. | Yes |
| 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). | Not applicable |
| 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. | Yes |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | Yes |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | Not applicable |
| Additional analysis | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | Yes |
| **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). | Yes |
| 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). | Yes |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | Yes |
| **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. | Yes |

*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

## 2. Search and selection strategy

PubMed, Embase and the Cochrane Central Register of Controlled Trials were queried using the search term [*"septic shock" AND (random* or rct)*]. Embase was additionally queried using the search term “septic shock” with the randomized controlled trial filter. The queries were limited to publications from 01-01-2006 and the queries were last performed on January 20, 2018. The list of excluded trials is appended at the end of this supplementary materials document.



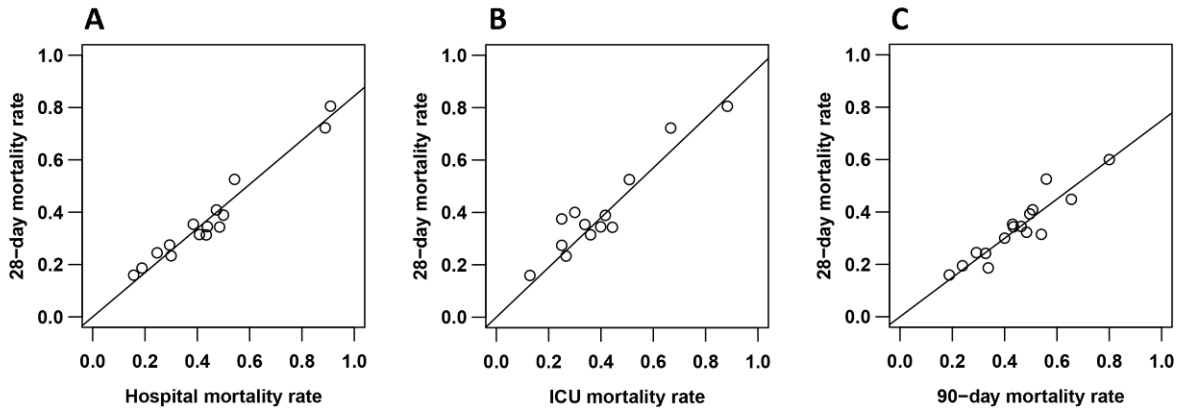

**eFigure 1.** Results of the search and selection strategy. * Irrelevant search results were reports that were clearly and unambiguously irrelevant to the research question for a variety of reasons (too many to count individually). These reasons included, but were not limited to: Animal studies, other preclinical studies, healthy volunteer studies and letters. Authors of trials that did not report mortality or baseline characteristics were not contacted for additional information.

### 3. Estimation of 28-day mortality from other mortality measures

For the 20 trials that did not report 28-day mortality, we estimated 28-day mortality based on reported hospital, ICU or 90-day mortality using linear regression with data from trials that reported both 28-day and another mortality measure.

**eTable 1. Equations used to estimate 28-day mortality.**

| Predictor | Trials estimated using predictor (n) | Trials used to derive prediction equation (n) | Prediction equation | P-value and $R^2$ value of prediction equation |
|---|---|---|---|---|
| Hospital mortality | 9 | 14 | 28-day = 0.84 x hospital | P<0.0001 R2=0.99 |
| ICU mortality | 10 | 13 | 28-day = 0.95 x ICU | P<0.0001 R2=0.98 |
| 90-day mortality | 1 | 18 | 28-day = 0.78 x 90-day | P<0.0001 R2=0.98 |




**eFigure 2.** Regression estimation plots of 28-day mortality from (A) hospital mortality, (B) ICU mortality and (C) 90-day mortality.

**4. Mean mortality rates and heterogeneity in subcategories of trials.**

**eTable 2. Estimation of mean mortality rates and heterogeneity of trial design and quality**

| | N (%) | Mean mortality (95% confidence interval) | τ: estimated heterogeneity (p-value) | 95% prediction interval |
|---|---|---|---|---|
| **All RCTs** | **65 (100)** | **38.6% (34.2 – 43.3%)** | **0.710 (<0.001)** | **13.5 – 71.7%** |
| Smallest 50% trials * | 32 (49) | 43.0% (36.0 – 50.4%) | 0.712 (<0.001) | 15.7 – 75.3% |
| Largest 50% trials * | 33 (51) | 35.5% (30.2 – 41.2%) | 0.676 (<0.001) | 12.7 – 67.5% |
| Monocenter trials | 37 (57) | 46.0% (39.0 – 53.3%) | 0.802 (<0.001) | 15.0 – 80.4% |
| Multicenter trials | 28 (43) | 30.6% (27.3 – 34.2%) | 0.376 (<0.001) | 17.4 – 48.0% |
| Unblinded trials | 41 (65) | 36.8% (31.5 – 42.6%) | 0.694 (<0.001) | 13.0 – 69.5% |
| Double-blind trials | 23 (35) | 42.4% (34.8 – 50.5%) | 0.725 (<0.001) | 15.1 – 75.3% |
| Trials with Jadad score ≤ 3 | 46 (71) | 39.5% (33.9 – 45.5%) | 0.760 (<0.001) | 12.9 – 74.4% |
| Trials with Jadad score > 3 | 18 (29) | 36.3% (30.0 – 43.0%) | 0.555 (<0.001) | 16.1 – 62.8% |
| Trials without usual-care control group | 14 (21) | 36.1% (29.9 – 43.0%) | 0.413 (<0.001) | 20.1 – 55.9% |
| Trials with usual-care control group | 51 (79) | 39.3% (34.0 – 44.8%) | 0.756 (<0.001) | 12.8 – 74.0% |

Mean mortality and heterogeneity parameters were estimated using a weighted random-effects model with mortality on the log-odds scale. Mortality was back-transformed from log-odds to percentages for clarity. The value of τ represents the estimated between-trial standard deviation in mortality on the log-odds scale. The 95% confidence intervals indicate the precision of the estimated mean, while the 95% prediction intervals represents the estimated between-trial variability in mortality rates after adjusting for random chance and sample size (equal to the mean mortality rate ± 1.96 τ on the log-odds scale). There was significant heterogeneity in all subcategories of trials. * The median sample size separating the 50% largest from smallest trials was 36 patients.

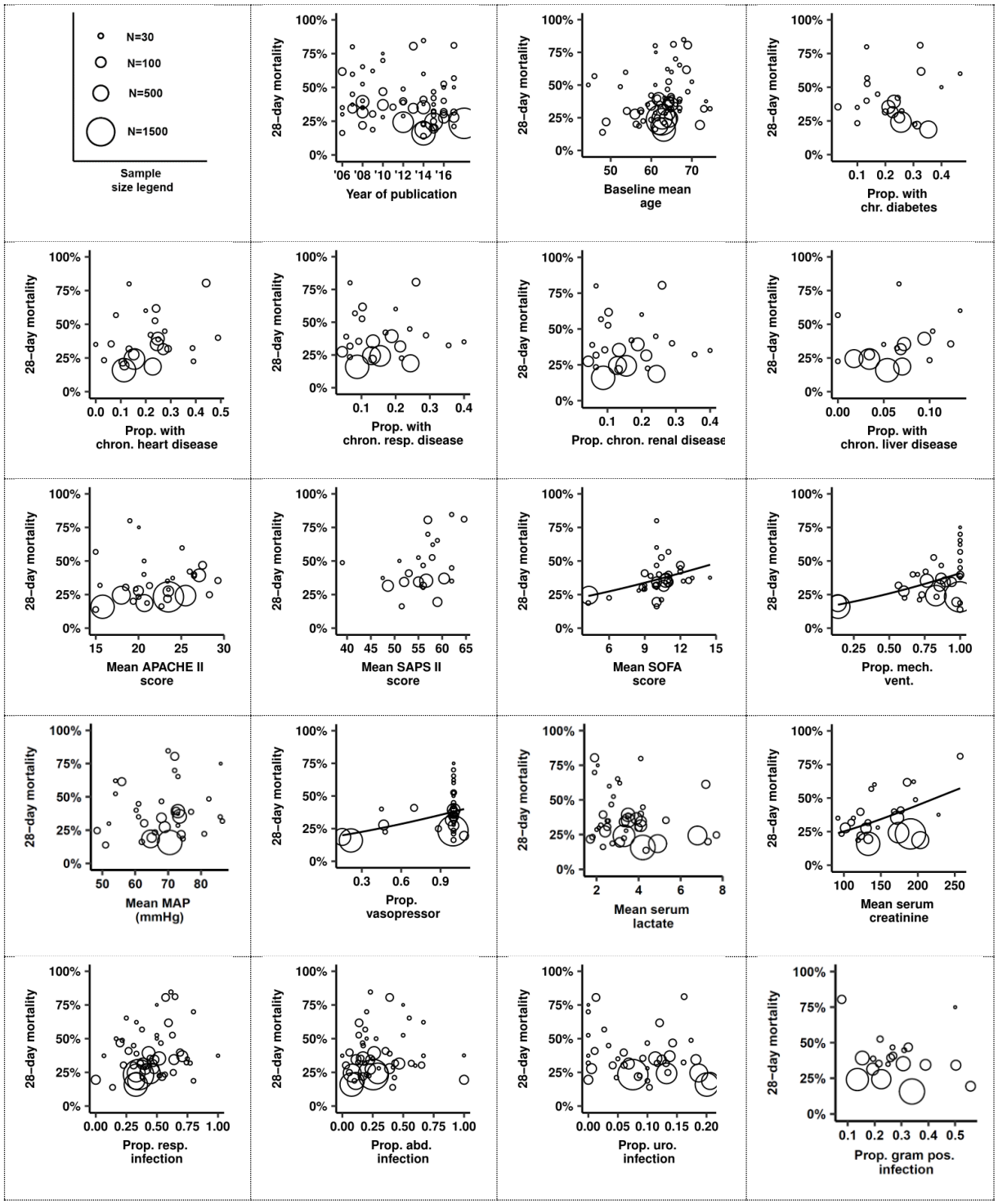
## 5. Regression goodness-of-fit statistics.

### eTable 3. Univariate regression goodness-of-fit statistics.

| | N (%) | Log-linear model AIC | Quadratic model AIC | Power model AIC | Model choice |
|---|---|---|---|---|---|
| Publication year | 65 (100) | 148.3 | 149.0 | 149.0 | Linear |
| | | | | | |
| Age, years | 64 (98) | 156.8 | 158.0 | 158.5 | Linear |
| Male patients % | 63 (97) | 145.0 | 155.0 | 158.5 | Linear |
| Comorbidity characteristics | | | | | |
| Charlson comorbidity index | 5 (8) | 14.1 | 14.9 | 14.5 | Linear |
| From long-term care facility % | 6 (9) | 11.9 | 13.9 | 11.9 | Linear |
| McCabe class I % | 6 (9) | 13.4 | 13.4 | 13.4 | Linear |
| McCabe class II % | 6 (9) | 14.2 | 15.5 | 14.2 | Linear |
| McCabe class III % | 4 (6) | 11.6 | 11.9 | 11.6 | Linear |
| Diabetes mellitus % | 23 (36) | 59.0 | 60.2 | 59.0 | Linear |
| Heart failure or coronary disease % | 26 (40) | 64.8 | 66.8 | 64.8 | Linear |
| Chronic obstructive pulmonary disease % | 25 (39) | 60.7 | 64.7 | 63.7 | Linear |
| Chronic renal disease % | 21 (33) | 54.5 | 55.3 | 54.6 | Linear |
| Chronic liver disease % | 17 (26) | 42.0 | 42.6 | 42.0 | Linear |
| Cancer % | 20 (31) | 54.6 | 56.6 | 54.6 | Linear |
| Severity of illness scores | | | | | |
| APACHE II score | 33 (51) | 74.1 | 75.9 | 74.6 | Lineaer |
| APACHE III score | 1 (2) | - | - | - | |
| APACHE IV score | 1 (2) | - | - | - | |
| SAPS II score | 24 (37) | 63.0 | 63.0 | 64.5 | Linear |
| SAPS III score | 3 (4) | 3.09 | 3.09 | 3.09 | Linear |
| SOFA score | 37 (58) | 57.9 | 59.4 | 63.7 | Linear |
| Characteristics of acute illness | | | | | |
| Medical (non-surgical) % | 22 (34) | 43.7 | 43.7 | 43.7 | Linear |
| Time from diagnosis to randomization, hours | 13 (20) | 29.5 | 31.5 | 29.5 | Linear |
| Mechanical ventilation % | 33 (51) | 64.2 | 66.3 | 64.4 | Linear |
| Heart rate, 1/min | 39 (60) | 107.8 | 109.8 | 107.8 | Linear |
| Mean arterial pressure, mmHg | 43 (66) | 111.6 | 113.5 | 111.7 | Linear |
| Central venous pressure, mmHg | 22 (34) | 68.2 | 96.7 | 68.6 | Linear |
| Vasopressor support % | 38 (58) | 71.6 | 71.8 | 72.0 | Linear |
| Serum lactate, mmol/L | 52 (80) | 130.8 | 131.9 | 131.3 | Linear |
| Serum creatinine, µmol/L | 26 (40) | 54.7 | 57.7 | 58.7 | Linear |
| Fluids before randomization, mL | 19 (30) | 44.4 | 46.4 | 46.3 | Linear |
| Infection site characteristics | | | | | |
| Respiratory % | 53 (82) | 128.5 | 130.3 | 128.7 | Linear |
| Abdominal % | 51 (78) | 122.1 | 122.1 | 122.2 | Linear |
| Urogenital % | 41 (63) | 97.8 | 99.6 | 97.9 | Linear |
| Central nervous system % | 19 (30) | 62.7 | 62.7 | 62.7 | Linear |
| Skin and soft tissue % | 28 (43) | 85.1 | 86.5 | 85.1 | Linear |
| Bloodstream % | 32 (49) | 82.7 | 83.8 | 82.8 | Linear |
| Pathogen characteristics | | | | | |
| Gram-negative % | 25 (39) | 58.6 | 59.9 | 58.9 | Linear |
| Gram-positive % | 22 (34) | 54.4 | 55.4 | 54.7 | Linear |
| Other pathogen % | 22 (34) | 55.8 | 56.7 | 56.4 | Linear |
| Culture negative % | 18 (28) | 35.6 | 36.3 | 35.6 | Linear |

The model with the smallest AIC (Akaike Information Criterion, which penalized additional regressors) was chosen. For equal AIC's, the linear model was preferred.

## 6. Plots of the association between baseline variables and mortality




**eFigure 3.** Associations between control group mortality and selected population characteristics. Circle sizes are proportional to the trial sample sizes. The lines represent significant linear associations estimated using inverse variance weighted random-effects model with mortality on the log-odds scale. Morality rates are back-transformed to percentages for clarity. APACHE, Acute Physiology and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment score; MAP, mean arterial pressure

**7. Results from multivariate linear model**

To estimate the proportion of heterogeneity that can be explained by a combination of population characteristics, we constructed a weighted multivariate random-effects linear model with multiple imputation to account for missing values.

Population variables that were reported by at least 25% of the included trials with a univariate regression $R^2 \geq 0.10$ were candidate regressors: The proportion of patients with chronic heart disease, mean SAPS-II score, mean SOFA score, the proportion of patients on mechanical ventilation, the proportion of patients on vasopressors, mean serum creatinine, the amount of fluids before randomization, the proportion of Gram-positive infections and the proportion of culture-negative infections.

Multiple imputation (generating 20 datasets) with predictive mean matching was used to estimate missing observations from the candidate variables. In addition to the candidate regressors above, population variables that were reported by more than 50% of trials were included in the multiple imputation datasets to strengthen the validity of the imputation: The year of publication, mean age, the proportion of male patients, mean APACHE II score, mean mean arterial pressure, mean heart rate, mean serum lactate, and the proportions of patients with respiratory, abdominal and urological infections. These variables were included in the imputation but not in the multivariate regression analysis.

Candidate variables that were eliminated stepwise from the model (for P≥0.05) were, in order of elimination: The amount of fluids before randomization (P=0.779), the proportion of patients on vasopressors (P=0.528), the proportion of Gram-negative cultures (P=0.712), the proportion of culture-negative infections (P=0.366), the proportion of patients with chronic heart disease (P=0.132), the proportion of Gram-positive cultures (P=0.126), mean SAPS-II score (P=0.102).

The final model estimating the effect of the independent variables on control-group 28-day mortality (expressed on the log-odds scale) was:

**eTable 4. Results from multivariate random-effects linear model**

| | coefficient | 95% confidence interval | | Std. Error | Std. coef. β | Std. Std. err | Z-value | P-value |
|---|---|---|---|---|---|---|---|---|
| Intercept | -3.341 | -4.409 | -2.274 | 0.544 | | | -6.134 | <0.0001 |
| Mean SOFA score | 0.103 | 0.017 | 0.189 | 0.044 | 0.389 | 0.166 | 2.343 | 0.0191 |
| Mechanical ventilation (%) | 0.979 | 0.162 | 1.797 | 0.417 | 0.422 | 0.179 | 2.348 | 0.0188 |
| Serum creatinine, µmol/L | 0.007 | 0.002 | 0.011 | 0.002 | 0.316 | 0.099 | 3.175 | 0.0015 |

Mixed effects model (k=65; $Tau^2$ estimator: Maximum Likelihood) $Tau^2 = 0.2955447$; Tau = 0.5436402;
Test for Residual Heterogeneity: QE(df = 61) = 685.7083, p-val < .0001
$R^2 = 0.4144$, residual $I^2$=81.9%
Estimated function: *Logodds(mortality rate) = -3.341 + 0.103 × [mean SOFA score] + 0.979 × [% mechanical ventilation] + 0.007 × [mean serum creatinine, µmol/L]*

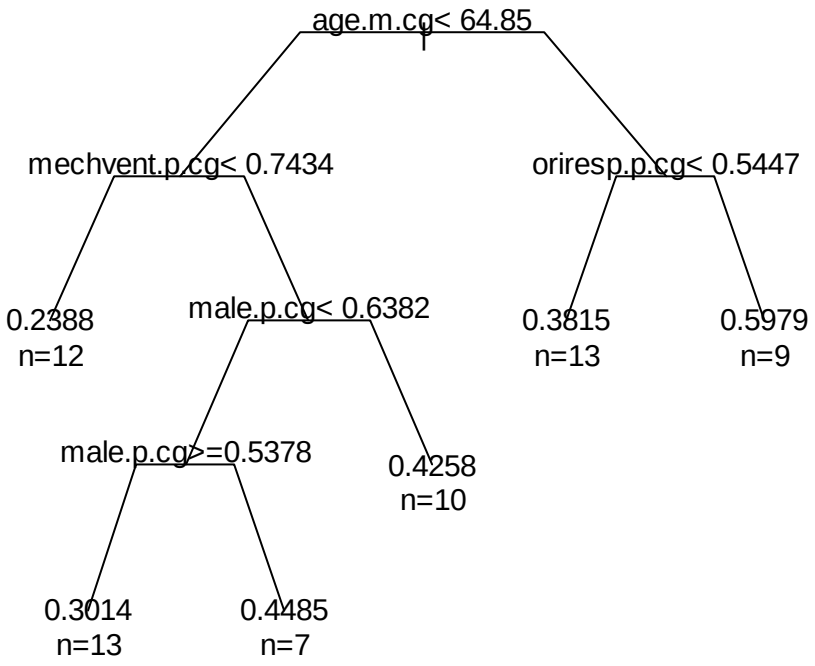
**8. Results from regression tree analysis.**

We constructed a regression tree using the Recursive Partitioning and Regression Tree (RPART) routines implemented in R (1, 2).

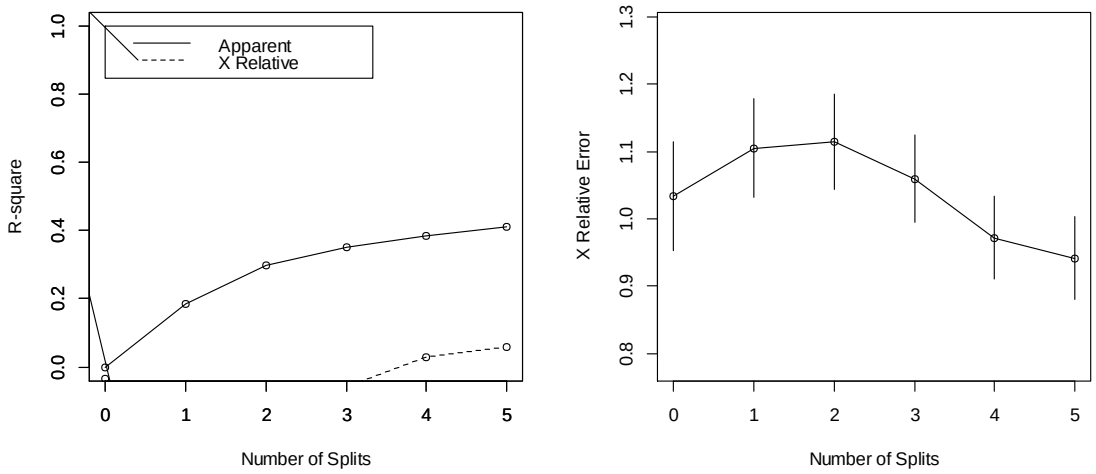
The dependent variable in the model was 28-day mortality. The recursive partitioning algorithm selected among all inclusion criteria and baseline characteristics the most informative variable, which was then 'split' at the value that best differentiates low- versus high mortality. The algorithm then selected the most informative variable for each of the two resulting subgroups, and split it again. When a splitting variable was missing for a specific trial, a surrogate variable (the variable most closely correlated to the splitting variable) was used.

The resulting regression tree is shown in eFigure 4. The cumulative proportion of variability in 28-day mortality explained the regression tree is ($R^2$) is 0.43 (eFigure 5, left panel). The cross-validated relative error decreased to below the the root (split 0) value, which indicates that the tree is likely not overfitted. (eFigure 5, right panel).

The algorithm output with primary splits and surrogate splits for missing values can be found at the end on this section.




**eFigure 4.** Regression tree for the prediction of 28-day mortality rate. The values between each terminal branch are the mean mortality rates for the n trials in the terminal branch. The splitting variables are: mean age (split at 64.8 years); the proportion of patients with a respiratory infection (split at 54.5%); the proportion of patients on mechanical ventilation (split at 74.3%); and the proportion of male patients (splits at 63.8% and 53.8%). The terminal numbers represent the mean mortality rate (and n number of trials) for that tree branch.




**eFigure 5.** The cumulative proportion of variability in 28-day mortality explained at each split ($R^2$, left panel) and the cross-validated relative error at each split (right panel). The $R^2$ for the whole tree is 0.42. The cross-validated relative error decreases to below the the root (split 0) value, which indicates that the tree is likely not overfitted.

R output:

rpart(formula = f, data = d, weights = sqrt(mort.cg.n), control = list(minsplit = 10))

n= 65

Node number 1: 64 observations, complexity param=0.1677901
mean=0.354528, MSE=0.02436645
left son=2 (42 obs) right son=3 (22 obs)
Primary splits:
age.m.cg < 64.85 to the left, improve=0.1770292, (1 missing)
Surrogate splits:
male.p.cg < 0.678044 to the left, agree=0.747, adj=0.066, (1 split)

Node number 2: 42 observations, complexity param=0.09663411
mean=0.3160983, MSE=0.01539218
left son=4 (12 obs) right son=5 (30 obs)
Primary splits:
mechvent.p.cg < 0.7434334 to the left, improve=0.1826555, (19 missing)
Surrogate splits:
population.incl.hyperlactatemia < 0.5 to the right, agree=0.862, adj=0.618, (19 split)

Node number 3: 22 observations, complexity param=0.1184911
mean=0.4609157, MSE=0.03380377
left son=6 (13 obs) right son=7 (9 obs)
Primary splits:
oriresp.p.cg < 0.5447349 to the left, improve=0.32381720, (4 missing)
Surrogate splits:
oriabd.p.cg < 0.1540171 to the right, agree=0.741, adj=0.378, (2 split)
year < 2013.5 to the right, agree=0.679, adj=0.229, (2 split)

Node number 4: 12 observations
mean=0.2388055, MSE=0.005242482

Node number 5: 30 observations,  complexity param=0.04253843
  mean=0.3575663, MSE=0.01591277
  left son=10 (20 obs) right son=11 (10 obs)
  Primary splits:
    male.p.cg  < 0.6381818 to the left,  improve=0.09969404, (1 missing)
  Surrogate splits:
    population.incl.mechanical.ventilation < 0.5  to the left,  agree=0.772, adj=0.186, (1 split)

Node number 6: 13 observations
  mean=0.3814903, MSE=0.0120705

Node number 7: 9 observations
  mean=0.5979004, MSE=0.0416422

Node number 10: 20 observations,  complexity param=0.04253843
  mean=0.3317222, MSE=0.0139477
  left son=20 (13 obs) right son=21 (7 obs)
  Primary splits:
    male.p.cg  < 0.537751  to the right, improve=0.23640110, (1 missing)
  Surrogate splits:
    year  < 2014.5  to the left,  agree=0.791, adj=0.013, (1 split)

Node number 11: 10 observations
  mean=0.4258359, MSE=0.01467858

Node number 20: 13 observations
  mean=0.3013633, MSE=0.004979949

Node number 21: 7 observations
  mean=0.4484868, MSE=0.0312601

**References**


1. Atkinson EJ, Therneau TM. An introduction to recursive partitioning using the RPART routines. *Rochester Mayo Found* 2017;
2. Therneau T, Atkinson B, Ripley B. rpart: Recursive Partitioning and Regression Trees. *R Packag version 41-11* 2017;

**9. List of excluded trials**

This list contains the search results that were deemed possibly relevant (evaluated in full text) but which were excluded for the reasons stated below.

| Search result | Reason for exclusion |
|---|---|
| Abd El Halim et al. Impact of gelatins on perfusion of microcirculatory blood flow in patient with septic shock. Intensive Care Medicine Experimental 2016;4 | Population includes sepsis / severe sepsis (not only shock) |
| Agrawal et al. Comparative study of dopamine and norepinephrine in the management of septic shock. Saudi Journal of Anaesthesia 2011;5(2):162-166 | No mortality outcome reported |
| Aguilar Arzapalo et al. Methylene blue effectiveness as contributory treatment in patients with septic shock. Intensive Care Medicine Experimental 2016;4 | Post-hoc secondary analysis or conference abstract |
| Alhashemi et al. Levosimendan vs dobutamine in septic shock. Journal of Critical Care 2009;24(3):e14-e15 | Post-hoc secondary analysis or conference abstract |
| Annane et al. Effect of low doses of corticosteroids in septic shock patients with or without early acute respiratory distress syndrome. Critical Care Medicine 2006;34(1):22-30 | Post-hoc secondary analysis or conference abstract |
| Asfar et al. Hyperoxia and hypertonic saline in patients with septic shock (HYPERS2S): a two-by-two factorial, multicentre, randomised, clinical trial. The Lancet Respiratory Medicine 2017;5(3):180-190 | Factorial design |
| Bergamin et al. Transfusion requirements in septic shock patients: A randomized controlled trial. Critical Care 2015 | Post-hoc secondary analysis or conference abstract |
| Caironi et al. Circulating Biologically Active Adrenomedullin (bio-ADM) Predicts Hemodynamic Support Requirement and Mortality During Sepsis. Chest 2017;152(2):312-320 | Post-hoc secondary analysis or conference abstract |
| Caironi et al. Pentraxin 3 in patients with severe sepsis or shock: the ALBIOS trial. European Journal of Clinical Investigation 2017;47(1):73-83 | Post-hoc secondary analysis or conference abstract |
| Capoletto et al. Vasopressin versus norepinephrine for the management of septic shock in cancer patients (vancs II). Critical Care 2017;21(1): | Specific subpopulation of septic shock |
| Cherfan et al. Etomidate and mortality in cirrhotic patients with septic shock.. BMC clinical pharmacology 2011;11():22 | Post-hoc secondary analysis or conference abstract |
| Choudhury et al. A randomized trial comparing terlipressin and noradrenaline in patients with cirrhosis and septic shock. | Specific subpopulation of septic shock |

| Search result | Reason for exclusion |
|---|---|
| Choudhury et al. A randomized trial comparing terlipressin and noradrenaline in patients with cirrhosis and septic shock. Liver International 2017;37(4):552-561 | Specific subpopulation of septic shock |
| Chung et al. High-volume hemofiltration in adult burn patients with septic shock and acute kidney injury: A multicenter randomized controlled trial. Critical Care 2017;21(1) | Specific subpopulation of septic shock |
| Clem et al. Norepinephrine and vasopressin vs norepinephrine alone for septic shock: Randomized controlled trial. Critical Care Medicine 2016;44(12):413 | Post-hoc secondary analysis or conference abstract |
| Cota-Delgado et al. Hemofiltration veno-venous continouos high and very high volume, pulmonary (paO2/FiO2) function and mortality in refractory septic shock patients. Intensive Care Medicine Experimental 2017;5(2): | Post-hoc secondary analysis or conference abstract |
| Cota-Delgado et al. Hemofiltration veno-venous continouos high and very high volume, hemodynamic answer and mortality in refractory septic shock patients. Intensive Care Medicine Experimental 2016;4 | Post-hoc secondary analysis or conference abstract |
| Coudroy et al. Modulation by Polymyxin-B Hemoperfusion of Inflammatory Response Related to Severe Peritonitis.. Shock (Augusta, Ga.) Aug 2016;(): | Post-hoc secondary analysis or conference abstract |
| Cronhjort et al. Association between fluid balance and mortality in patients with septic shock: a post hoc analysis of the TRISS trial.. Acta anaesthesiologica Scandinavica Aug 2016;60(7):925-33 | Post-hoc secondary analysis or conference abstract |
| Cronhjort et al. Association between fluid balance and mortality in patients with septic shock: A post hoc analysis of the TRISS trial. Acta Anaesthesiologica Scandinavica 2016 | Post-hoc secondary analysis or conference abstract |
| Cuthbertson et al. The effects of etomidate on adrenal responsiveness and mortality in patients with septic shock.. Intensive care medicine 2009;35(11):1868-1876 | Post-hoc secondary analysis or conference abstract |
| David et al. Therapeutic plasma exchange as rescue therapy in refractory septic shock. Infection 2017;45(1):S46 | Post-hoc secondary analysis or conference abstract |
| Davis et al. Prognostic value of peripheral venous oxygen tension to predict an abnormal initial central venous oxygen saturation in emergency department patients undergoing quantitative resuscitation for septic shock. Academic Emergency Medicine 2012;19 | Post-hoc secondary analysis or conference abstract |
| De Winter et al. Higher versus standard amikacin single dose in emergency department patients with severe sepsis and shock: a randomized controlled trial.. International journal of antimicrobial agents Nov 2017 | Population includes sepsis / severe sepsis (not only shock) |
| Deans et al. Intensive insulin therapy did not reduce mortality more than conventional therapy in septic shock treated with corticosteroids. Annals of Internal Medicine 2010;152(10):JC5-5 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Delbove et al. Impact of endotracheal intubation on septic shock outcome: A post hoc analysis of the SEPSISPAM trial.. Journal of critical care Dec 2015;30(6):1174-8 | Post-hoc secondary analysis or conference abstract |
| Dhainaut et al. Extended drotrecogin alfa (activated) treatment in patients with prolonged septic shock. | Specific subpopulation of septic shock |
| Dhifaoui et al. On-line hemofltration versus conventional hemofltration in septic shock patients: Clinical safety and effectiveness. Annals of Intensive Care 2017;7(1):114 | Specific subpopulation of septic shock |
| Elbaradey et al. The effect of atrial natriuretic peptide infusion on intestinal injury in septic shock. Journal of Anaesthesiology Clinical Pharmacology 2016;32(4):470-475 | Specific subpopulation of septic shock |
| Ferrario et al. Mortality prediction in patients with severe septic shock: a pilot study using a target metabolomics approach. Scientific reports 2016;6 | Post-hoc secondary analysis or conference abstract |
| Fisher et al. Heparin-Binding Protein (HBP): A Causative Marker and Potential Target for Heparin Treatment of Human Sepsis-Induced Acute Kidney Injury.. Shock (Augusta, Ga.) Sep 2017;48(3):313-320 | Post-hoc secondary analysis or conference abstract |
| Forceville Effects of high doses of selenium, as sodium selenite, in septic shock patients a placebo-controlled, randomized, double-blind, multi-center phase II study--selenium and sepsis.. Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS) 2007;21 Suppl 1():62-5 | Post-hoc secondary analysis or conference abstract |
| Galstyan et al. Administration of multipotent mesenchymal stromal cells (MSC) improves short term but not long term survival in oncohematological neutropenic patients (PTS) with septic shock (SS). Intensive Care Medicine Experimental 2016;4 | Specific subpopulation of septic shock |
| Gaudry et al. Effect of renal replacement therapy strategies in septic-shock patients with severe acute kidney injury: A post hoc analysis of a randomized controlled trial. Annals of Intensive Care 2017;7(1):5 | Post-hoc secondary analysis or conference abstract |
| Gaudry et al. Initiation strategies for renal replacement therapy according to severity and septic shock: A post-hoc analysis of the akiki trial. American Journal of Respiratory and Critical Care Medicine 2017;195 | Specific subpopulation of septic shock |
| Gordon et al. The cardiopulmonary effects of vasopressin compared with norepinephrine in septic shock.. Chest Sep 2012;142(3):593-605 | Post-hoc secondary analysis or conference abstract |
| Gordon et al. The effects of vasopressin on acute kidney injury in septic shock. Intensive Care Medicine 2010;36(1):83-91 | Post-hoc secondary analysis or conference abstract |
| Guo-Long et al. The effects of the Qingre Jiedu Tongfu recipe on adjunct therapy in septic shock patients from ICU-a multicenter perspective randomized controlled study. Intensive Care Medicine 2014;40(1):S213 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Haase et al. Thromboelastography in patients with severe sepsis: a prospective cohort study.. Intensive care medicine Jan 2015;41(1):77-85 | Post-hoc secondary analysis or conference abstract |
| Haddad et al. Association of preservative-free propofol use and outcome in critically ill patients. American Journal of Infection Control 2011;39(2):141-147 | Post-hoc secondary analysis or conference abstract |
| Hajjej et al. Effects of continuous haemofltration versus intermittent haemodialysis on microcirculatory parameters in septic shock: A muscle microdialysis study. Annals of Intensive Care 2017;7(1):153 | Specific subpopulation of septic shock |
| Harvey et al. Effect of heart rate control with esmolol on haemodynamic and clinical outcomes in patients with septic shock 2C03, 3C00. Journal of the Intensive Care Society 2014;15(3):262-263 | Post-hoc secondary analysis or conference abstract |
| Hjortrup et al. Effects of fluid restriction on measures of circulatory efficacy in adults with septic shock. Acta Anaesthesiologica Scandinavica 2017;61(4):390-398 | Post-hoc secondary analysis or conference abstract |
| Holst et al. Lower versus higher hemoglobin threshold for transfusion in septic shock.. | Specific subpopulation of septic shock |
| Holst Benefits and harms of red blood cell transfusions in patients with septic shock in the intensive care unit.. Danish medical journal Feb 2016;63(2): | Post-hoc secondary analysis or conference abstract |
| Hou et al. Endothelial Permeability and Hemostasis in Septic Shock: Results From the ProCESS Trial. Chest 2017;152(1):22-31 | Post-hoc secondary analysis or conference abstract |
| Hsieh et al. Prevalence and impact of active and passive cigarette smoking in acute respiratory distress syndrome. Critical Care Medicine 2014;42(9):2058-2068 | Post-hoc secondary analysis or conference abstract |
| Hussain et al. Efficacy of phenylephrine versus noradrenaline in management of patients presenting with septic shock in the intensive care unit. Rawal Medical Journal 2014;39(2):136-140 | No mortality outcome reported |
| Jaoued et al. Effect of mode of hydrocortisone administration in patients with septic shock: A prospective randomized trial. Annals of Intensive Care 2017;7(1):151-152 | Post-hoc secondary analysis or conference abstract |
| Joannes-Bayou et al. High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial.. | Specific subpopulation of septic shock |
| Johansen et al. Mild induced hypothermia: Effects on sepsis-related coagulopathy -results from a randomized controlled trial. Thrombosis Research 2015;135(1):175-182 | Post-hoc secondary analysis or conference abstract |
| Johansson et al. Association between sympathoadrenal activation, fibrinolysis, and endothelial damage in septic patients: a prospective study.. Journal of critical care Jun 2014;29(3):327-33 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Kadoi et al. Comparative effects of propofol vs dexmedetomidine on cerebrovascular carbon dioxide reactivity in patients with septic shock.. British journal of anaesthesia Feb 2008;100(2):224-9 | No mortality outcome reported |
| Kaufmann et al. Stress doses of hydrocortisone in septic shock: Beneficial effects on opsonization-dependent neutrophil functions. Intensive Care Medicine 2008;34(2):344-349 | No mortality outcome reported |
| Kawazoe et al. Effect of PMX-DHP longer than 2 hours on mortality in patients with septic shock: A sub-analysis of multicenter randomized controlled trial. Intensive Care Medicine Experimental 2017;5(2): | Post-hoc secondary analysis or conference abstract |
| Kellum et al. Relationship between Alternative Resuscitation Strategies, Host Response and Injury Biomarkers, and Outcome in Septic Shock: Analysis of the Protocol-Based Care for Early Septic Shock Study. Critical Care Medicine 2017;45(3):438-445 | Post-hoc secondary analysis or conference abstract |
| Kellum et al. The Effects of Alternative Resuscitation Strategies on Acute Kidney Injury in Patients with Septic Shock.. American journal of respiratory and critical care medicine Feb 2016;193(3):281-7 | Post-hoc secondary analysis or conference abstract |
| Kiehntopf et al. Prognostic impact of procalcitonin in severe sepsis and septic shock results of the VISEP-study. Infection 2011;39 | Post-hoc secondary analysis or conference abstract |
| Kjaer et al. Factors associated with non-response at quality of life follow-up among survivors of septic shock. A registry-based post-hoc analysis of the TRISS randomised trial. Intensive Care Medicine Experimental 2017;5(2): | Post-hoc secondary analysis or conference abstract |
| Kjær et al. Factors associated with non-response at health-related quality of life follow-up in a septic shock trial. Acta Anaesthesiologica Scandinavica 2017 | Post-hoc secondary analysis or conference abstract |
| László et al. Effects of adsorption of cytokines early in septic shock (the 'acess-trial')-results of the pilot study. Critical Care 2017;21(1): | Post-hoc secondary analysis or conference abstract |
| Lauzier et al. Vasopressin or norepinephrine in early hyperdynamic septic shock: a randomized clinical trial.. | Specific subpopulation of septic shock |
| Laviolle et al. Gluco- and mineralocorticoid biological effects of a 7-day treatment with low doses of hydrocortisone and fludrocortisone in septic shock.. Intensive care medicine Aug 2012;38(8):1306-14 | Post-hoc secondary analysis or conference abstract |
| Li et al. Platelet desialylation is a novel mechanism and a therapeutic target in thrombocytopenia during sepsis: An open-label, multicenter, randomized controlled trial. Journal of Hematology and Oncology 2017;10(1): | Population includes sepsis / severe sepsis (not only shock) |
| Li et al. Platelet desialylation is a novel mechanism and a therapeutic target in thrombocytopenia during sepsis: An open-label, multicenter, randomized controlled trial. Haematologica 2017;102 | Population includes sepsis / severe sepsis (not only shock) |
| Liu et al. Clinical effect of alprostadil in patients with septic shock associated with acute respiratory distress syndrome. Medical Journal of Chinese People's Liberation Army 2017;42(9):805-809 | Specific subpopulation of septic shock |

| Search result | Reason for exclusion |
|---|---|
| Liu et al. Application strategy of PiCCO in septic shock patients.. Experimental and therapeutic medicine Apr 2016;11(4):1335-1339 | No mortality outcome reported |
| Mabasa et al. Full vs. renal dosing of antibiotics in septic shock patients with acute renal failure: The fraser feasibility trial. Critical Care Medicine 2009;37(12):A429 | Post-hoc secondary analysis or conference abstract |
| Masson et al. Presepsin (soluble CD14 subtype) and procalcitonin levels for mortality prediction in sepsis: data from the Albumin Italian Outcome Sepsis trial.. Critical care (London, England) 2014;18(1):R6 | Post-hoc secondary analysis or conference abstract |
| Masson et al. Sequential N-Terminal Pro-B-Type Natriuretic Peptide and High-Sensitivity Cardiac Troponin Measurements during Albumin Replacement in Patients with Severe Sepsis or Septic Shock. Critical Care Medicine 2016;44(4):707-716 | Post-hoc secondary analysis or conference abstract |
| Masson et al. Circulating presepsin (soluble CD14 subtype) as a marker of host response in patients with severe sepsis or septic shock: data from the multicenter, randomized ALBIOS trial. Intensive Care Medicine 2015;41(1):12-20 | Post-hoc secondary analysis or conference abstract |
| McIntyre et al. The PRECISE RCT: Evolution of an Early Septic Shock Fluid Resuscitation Trial. Transfusion Medicine Reviews 2012;26(4):333-341 | Post-hoc secondary analysis or conference abstract |
| McIntyre et al. Fluid Resuscitation with 5% albumin versus Normal Saline in Early Septic Shock: A pilot randomized, controlled trial. Journal of Critical Care 2012;27(3):317.e1-317.e6 | No baseline characteristics reported |
| McIntyre et al. The PRECISE fluid resuscitation pilot randomized controlled trial: Study design and preliminary feasibility results. American Journal of Respiratory and Critical Care Medicine 2010;181(1): | Post-hoc secondary analysis or conference abstract |
| McLaughlin et al. High versus low blood pressure target in patients with septic shock 2C03, 3C00. Journal of the Intensive Care Society 2014;15(3):258-259 | Post-hoc secondary analysis or conference abstract |
| Meddeb et al. Effects of levosimendan on cellular metabolic alterations in patients with septic shock: A randomised controlled study. Intensive Care Medicine Experimental 2015;3 | Post-hoc secondary analysis or conference abstract |
| Mehta et al. Cardiac ischemia in patients with septic shock randomized to vasopressin or norepinephrine. Critical Care 2013;17(3): | Post-hoc secondary analysis or conference abstract |
| Mehta et al. Agreement in electrocardiogram interpretation in patients with septic shock. Critical Care Medicine 2011;39(9):2080-2086 | Post-hoc secondary analysis or conference abstract |
| Memiş et al. The effects of levosimendan vs dobutamine added to dopamine on liver functions assessed with noninvasive liver function monitoring in patients with septic shock. Journal of Critical Care 2012;27(3):318.e1-318.e6 | No mortality outcome reported |
| Meng et al. Levosimendan Versus Dobutamine in Myocardial Injury Patients with Septic Shock: A Randomized Controlled Trial. | Specific subpopulation of septic shock |

| Search result | Reason for exclusion |
|---|---|
| Mishra et al. A pilot randomized controlled trial of comparison between extended daily hemodialysis and continuous veno-venous hemodialysis in patients of acute kidney injury with septic shock. Indian Journal of Critical Care Medicine 2017;21(5):262-267 | Specific subpopulation of septic shock |
| Miyamoto et al. Effect of Dexmedetomidine on Lactate Clearance in Patients with Septic Shock: A Sub-Analysis of a Multicenter Randomized Controlled Trial.. | Septic shock not defined according to commonly accepted criteria (3 cSOFA points). patients with septic shock under ventilation (sub-analysis of septic shock patients from larger trial including septic patient (not only shock)) |
| Molina et al. Are the low serum levels of vasopressin in septic shock patients refractory to catecholamines?. Intensive Care Medicine 2013;39 | Post-hoc secondary analysis or conference abstract |
| Morelli et al. Effects of vasopressinergic receptor agonists on sublingual microcirculation in norepinephrine-dependent septic shock. Critical Care 2011;15(5): | No mortality outcome reported |
| Moreno et al. Time course of organ failure in patients with septic shock treated with hydrocortisone: Results of the Corticus study. Intensive Care Medicine 2011;37(11):1765-1772 | Post-hoc secondary analysis or conference abstract |
| Moskowitz et al. Thiamine as a Renal Protective Agent in Septic Shock. A Secondary Analysis of a Randomized, Double-Blind, Placebo-controlled Trial.. Annals of the American Thoracic Society May 2017;14(5):737-741 | Post-hoc secondary analysis or conference abstract |
| Mouncey et al. Protocolised Management In Sepsis (ProMISe):A multicentre randomised controlled trial of the clinical effectiveness and cost-effectiveness of early, goal-directed, protocolised resuscitation for emerging septic shock. Health Technology Assessment 2015;19(97):1-150 | Post-hoc secondary analysis or conference abstract |
| Nguyen et al. Early lactate clearance is associated with biomarkers of inflammation, coagulation, apoptosis, organ dysfunction and mortality in severe sepsis and septic shock. Journal of Inflammation 2010;7 | Post-hoc secondary analysis or conference abstract |
| Park et al. Lactated Ringer Versus Albumin in Early Sepsis Therapy (RASP) study: Preliminary data of a randomized controlled trial. Critical Care 2015;19 | Post-hoc secondary analysis or conference abstract |
| Peake et al. Potential Impact of the 2016 Consensus Definitions of Sepsis and Septic Shock on Future Sepsis Research.. Annals of emergency medicine Oct 2017;70(4):553-561.e1 | Post-hoc secondary analysis or conference abstract |
| Permpikul et al. Early norepinephrine administration vs. standard treatment during severe sepsis/septic shock resuscitation: A randomized control trial. Intensive Care Medicine Experimental 2017;5(2): | Population includes sepsis / severe sepsis (not only shock) |

| Search result | Reason for exclusion |
|---|---|
| Perner et al. Hydroxyethyl starch 130/0.42 increased death at 90 days compared with Ringer's acetate in severe sepsis. Annals of Internal Medicine 2012;157(8):JC4-JC6 | Post-hoc secondary analysis or conference abstract |
| Philips et al. Comparison and outcomes of 5% albumin vs 0.9% normal saline fluid resuscitation in cirrhotics presenting with sepsis induced hypotension-a randomized controlled trial-fluid resuscitation in septic shock in cirrhosis (FRISC Protocol). Hepatology 2015;62((Mitra L.G.) Anesthesia and Critical Care, Institute of Liver and Biliary Sciences, New Delhi, India):261A | Post-hoc secondary analysis or conference abstract |
| Polito et al. Pharmacokinetics of oral fludrocortisone in septic shock.. British journal of clinical pharmacology Dec 2016;82(6):1509-1516 | Post-hoc secondary analysis or conference abstract |
| Polli et al. Effects of recombinant human activated protein C on the fibrinolytic system of patients undergoing conventional or tight glycemic control.. Minerva anestesiologica ;75(7-8):417-26 | Post-hoc secondary analysis or conference abstract |
| Póvoa et al. Clinical impact of stress dose steroids in patients with septic shock: insights from the PROWESS-Shock trial.. Critical care (London, England) 2015;19():193 | Post-hoc secondary analysis or conference abstract |
| Prakash et al. Early introduction of a combination of low dose terlipressin and noradrenaline as vasopressors is superior to high dose noradrenaline alone in patients of cirrhosis with septic shock(NCT02468063). Hepatology 2017;66 | Specific subpopulation of septic shock |
| Puskarich et al. Association between the timing of antibiotic administration and outcome in patients with septic shock. Academic Emergency Medicine 2011;18(5):S4 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Concordance and prognostic value of central venous oxygen saturation and lactate clearance of emergency department patients with septic shock. Academic Emergency Medicine 2011;18(5):S159-S160 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Pharmacometabolomics of L-carnitine treatment response phenotypes in patients with septic shock. Annals of the American Thoracic Society 2015;12(1):46-56 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Randomized controlled trial of safety and efficacy of l-carnitine infusion for the treatment of vasopressor-dependent septic shock. Academic Emergency Medicine 2013;20(5):S304 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Whole blood lactate kinetics in patients undergoing quantitative resuscitation for severe sepsis and septic shock. Chest 2013;143(6):1548-1553 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Prognostic value and agreement of achieving lactate clearance or central venous oxygen saturation goals during early sepsis resuscitation. Academic Emergency Medicine 2012;19(3):252-258 | Post-hoc secondary analysis or conference abstract |
| Puskarich et al. Association between timing of antibiotic administration and mortality from septic shock in patients treated with a quantitative resuscitation protocol. Critical Care Medicine 2011;39(9):2066-2071 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Puskarich et al. Outcomes of patients undergoing early sepsis resuscitation for cryptic shock compared with overt shock. Resuscitation 2011;82(10):1289-1293 | Post-hoc secondary analysis or conference abstract |
| Quraishi et al. Effect of cholecalciferol supplementation on vitamin d status and cathelicidin in sepsis. Critical Care Medicine 2014;42(12):A1383 | Post-hoc secondary analysis or conference abstract |
| Richard et al. Preload-dependence indices to titrate volume expansion during septic shock: A randomized controlled trial. Intensive Care Medicine 2014;40(1):S237 | Post-hoc secondary analysis or conference abstract |
| Rowan et al. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis.. The New England journal of medicine 06 2017;376(23):2223-2234 | Post-hoc secondary analysis or conference abstract |
| Rüddel et al. Effects of time to source control on 28-day-mortality in patients with severe sepsis or septic shock. Infection 2017;45(1):S49-S50 | Post-hoc secondary analysis or conference abstract |
| Russell et al. The Septic Shock 3.0 definition and trials: A vasopressin and Septic Shock trial experience. Critical Care Medicine 2017;45(6):940-948 | Post-hoc secondary analysis or conference abstract |
| Russell et al. Vasopressin compared with norepinephrine augments the decline of plasma cytokine levels in septic shock. American Journal of Respiratory and Critical Care Medicine 2013;188(3):356-364 | Post-hoc secondary analysis or conference abstract |
| Russell et al. Interaction of vasopressin infusion, corticosteroid treatment, and mortality of septic shock. Critical Care Medicine 2009;37(3):811-818 | Post-hoc secondary analysis or conference abstract |
| Rygård et al. Lower versus higher haemoglobin threshold for blood transfusion in septic shock: Exploratory subgroup analyses of a randomised trial. Intensive Care Medicine Experimental 2016;4 | Post-hoc secondary analysis or conference abstract |
| Rygård et al. Higher vs. lower haemoglobin threshold for transfusion in septic shock: subgroup analyses of the TRISS trial. Acta Anaesthesiologica Scandinavica 2017;61(2):166-175 | Post-hoc secondary analysis or conference abstract |
| Rygård et al. Long-term outcomes in patients with septic shock transfused at a lower versus a higher haemoglobin threshold: the TRISS randomised, multicentre clinical trial.. Intensive care medicine Nov 2016;42(11):1685-1694 | Post-hoc secondary analysis or conference abstract |
| Saoraya et al. Immunomodulation of therapeutic normothermia in febrile septic shock patients: A randomized controlled trial. Intensive Care Medicine Experimental 2017;5(2): | Post-hoc secondary analysis or conference abstract |
| Schädler et al. The effect of a novel extracorporeal cytokine hemoadsorption device on IL-6 elimination in septic patients: A randomized controlled trial. PLoS ONE 2017;12(10): | Population includes sepsis / severe sepsis (not only shock) |
| Schädler et al. Extracorporeal cytokine hemoadsorption in severely septic patients: A multicenter randomized controlled trial. Intensive Care Medicine 2013;39((Kuhlmann M.K.) Vivantes Hospital Friedrichshain, Berlin, Germany):S214 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Schortgen et al. Respective impact of lowering body temperature and heart rate on mortality in septic shock: mediation analysis of a randomized trial. Intensive Care Medicine 2015;41(10):1800-1808 | Post-hoc secondary analysis or conference abstract |
| Schortgen et al. External cooling reduces vasopressor use in septic shock: Preliminary results from the sepsiscool study. Intensive Care Medicine 2010;36 | Post-hoc secondary analysis or conference abstract |
| Schortgen et al. External cooling accelerates the weaning of vasopressors in septic shock. American Journal of Respiratory and Critical Care Medicine 2011;183(1) | Post-hoc secondary analysis or conference abstract |
| Scott et al. Lower versus higher haemoglobin threshold for transfusion in septic shock. Journal of the Intensive Care Society 2015;16(4):345-347 | Post-hoc secondary analysis or conference abstract |
| Semeraro et al. Platelet Drop and Fibrinolytic Shutdown in Patients With Sepsis.. Critical care medicine Dec 2017;(): | Post-hoc secondary analysis or conference abstract |
| Sharma et al. Incidence of acute respiratory distress syndrome from two study sites of the protocolized care for early septic shock trial. Academic Emergency Medicine 2017;24 | Post-hoc secondary analysis or conference abstract |
| Srisawat et al. The immunomodulation effect of Polymyxin-B Hemoperfusion in severe sepsis/septic shock: A randomized controlled trial. Intensive Care Medicine Experimental 2016;4 | Population includes sepsis / severe sepsis (not only shock) |
| Sterling et al. Organ dysfunction in survivors of septic shock treated with early quantitative resuscitation. Academic Emergency Medicine 2013;20(5):S285-S286 | Post-hoc secondary analysis or conference abstract |
| Thompson et al. Drotrecogin alfa (activated) did not reduce mortality at 28 or 90 days in patients with septic shock. Annals of Internal Medicine 2012;157(4):JC4-JC11 | Post-hoc secondary analysis or conference abstract |
| Toma et al. Steroids for patients in septic shock: The results of the CORTICUS trial. Canadian Journal of Emergency Medicine 2011;13(4):273-276 | Post-hoc secondary analysis or conference abstract |
| Tongyoo et al. Hydrocortisone in treatment of severe sepsis and septic shock with acute respiratory distress syndrome: A randomised controlled trial. Intensive Care Medicine Experimental 2015;3 | Post-hoc secondary analysis or conference abstract |
| Toth et al. Effects of IgM-enriched immunoglobulin therapy in septic-shock-induced multiple organ failure: pilot study.. | Specific subpopulation of septic shock |
| Venkatesh et al. The ADRENAL study protocol: adjunctive corticosteroid treatment in critically ill patients with septic shock.. Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine 2013;15(2):83-88 | Post-hoc secondary analysis or conference abstract |
| Wacharasint et al. One size does not fit all in severe infection: obesity alters outcome, susceptibility, treatment, and inflammatory response.. Critical care (London, England) 2013;17(3):R122 | Post-hoc secondary analysis or conference abstract |

| Search result | Reason for exclusion |
|---|---|
| Wacharasint et al. Normal-range blood lactate concentration in septic shock is prognostic and predictive. Shock 2012;38(1):4-10 | Post-hoc secondary analysis or conference abstract |
| Wiedermann et al. High-dose antithrombin III in the treatment of severe sepsis in patients with a high risk of death: Efficacy and safety. Critical Care Medicine 2006;34(2):285-292 | Post-hoc secondary analysis or conference abstract |
| Xiao et al. Effects of terlipressin on patients with sepsis via improving tissue blood flow. Journal of Surgical Research 2016;200(1):274-282 | No mortality outcome reported |
| Yang et al. Body temperature control in patients with refractory septic shock: too much may be harmful. | Specific subpopulation of septic shock |
| Yaseen et al. Low-dose hydrocortisone in patients with cirrhosis and septic shock: a randomized controlled trial.. | Specific subpopulation of septic shock |
| Yeh et al. The effect of endotoxin adsorber hemoperfusion on microcirculation in patients with severe sepsis and septic shock. Intensive Care Medicine Experimental 2015;3( | Population includes sepsis / severe sepsis (not only shock) |
| Yu et al. Global end-diastolic volume index vs central venous pressure goal-directed fluid resuscitation for chronic obstructive pulmonary disease patients with septic shock: a randomized controlled trial. | Specific subpopulation of septic shock |
| Yu et al. Global end-diastolic volume index vs CVP goal-directed fluid resuscitation for COPD patients with septic shock: a randomized controlled trial. American Journal of Emergency Medicine 2017;35(1):101-105 | Specific subpopulation of septic shock |
| Yune et al. Infusion of methylene blue in severe sepsis and septic shock: A randomized controlled trial. Critical Care Medicine 2016;44(12):439 | Population includes sepsis / severe sepsis (not only shock) |
| Zhang et al. Shenfu injection for improving cellular immunity and clinical outcome in patients with sepsis or septic shock. | Population includes sepsis / severe sepsis (not only shock) |
| Zhang et al. Sepsis endotypes and their physiologic characterization using vital signs. Critical Care Medicine 2016;44(12):408 | Post-hoc secondary analysis or conference abstract |
| Zhang et al. Identifying sepsis endotypes and time of onset from interleukin-6 trajectories in septic shock patients. Intensive Care Medicine Experimental 2016;4 | Post-hoc secondary analysis or conference abstract |
| Zhao et al. Pharmacokinetic and pharmacodynamic efficacies of continuous versus intermittent administration of meropenem in patients with severe sepsis and septic shock: A prospective randomized pilot study. Chinese Medical Journal 2017;130(10):1139-1145 | Population includes sepsis / severe sepsis (not only shock) |
| Zhu et al. Varying Presentations and Outcomes of Septic Shock: Should Septic Shock Be Stratified?. The American surgeon Nov 2017;83(11):1235-1240 | Post-hoc secondary analysis or conference abstract |