**Supplemental Electronic Material**

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6) Forest plot for SOFA score at day 7

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8) Meta-regression for short-term mortality outcome by control group mortality

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18) Sensitivity analysis for short-term mortality – excluding high risk or probably high risk of bias studies

19) Metaregression results (p-values for interaction) for subgroup analysis

**1) Supplemental Material. Search strategy for MEDLINE (Ovid SP)**

1. exp Sepsis/

2. exp Shock, Septic/

3. (sepsis or septic shock).mp.

4. 1 or 2 or 3

5. exp Adrenal Cortex Hormones/

6. (corticosteroid\* or steroid\*).mp.

7. 6 or 5

8. 4 and 7

9. ((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or clinical trials as topic.sh. or randomly.

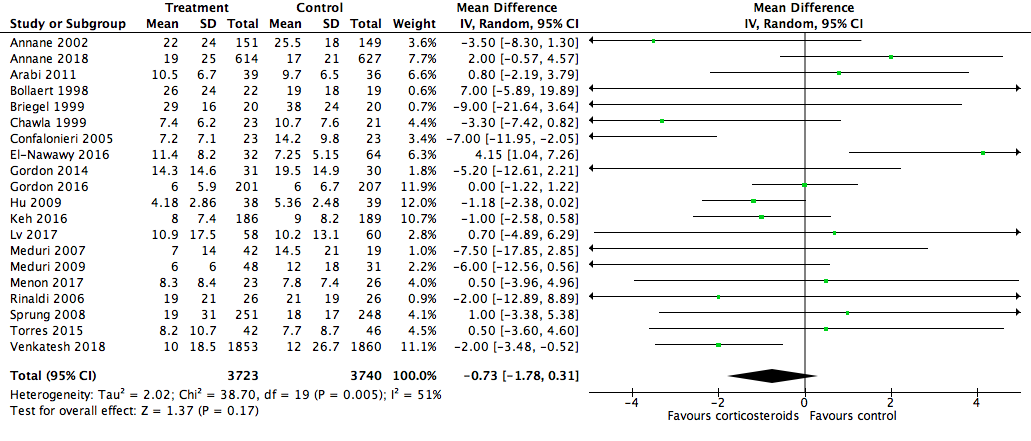
ab. or trial.ti.) not (animals not (humans and animals)).sh.

10. 8 and 9

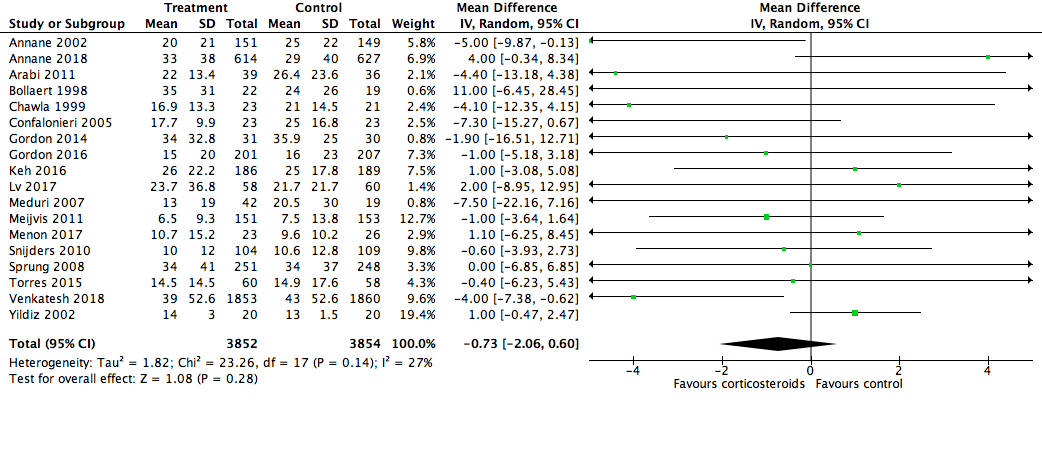
**2) Supplemental Table 1. Individual Study risk of bias assessment.**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Study**  **(author, year)** | **Randomization Generation** | **Allocation Concealment** | **Blinding** | **Incomplete Data** | **Selective Reporting** | **Other** | **Overall ROB** |
| **Annane 2002** | low | low | low | low | low | low | low |
| **Annane 2018** | low | low | low | low | low | low | low |
| **Arabi 2011** | low | low | low | probably low | probably low | low | probably low |
| **Bollaert 1998** | low | low | low | low | low | probably high | probably high |
| **Bone 1987** | low | low | low | low | probably low | probably low | probably low |
| **Branco 2014** | probably low | probably low | probably low | probably low | probably high | high | high |
| **Briegel 1999** | Low | low | low | low | probably low | low | probably low |
| **Chawla 1999** | low | low | low | low | low | low | low |
| **Cicarelli 2007** | probably high | low | low | probably low | probably low | probably low | probably high |
| **Confalonieri 2005** | low | low | low | high | low | high | high |
| **CSG 1963** | probably low | probably low | probably low | low | probably high | probably low | probably high |
| **DeGraaf 2014** | probably low | probably low | probably high | probably high | probably low | low | probably high |
| **El-Nawawy 2016** | low | low | low | probably high | probably high | low | probably high |
| **Gordon 2014** | low | low | probably low | probably low | low | low | probably low |
| **Gordon 2016** | low | low | low | low | low | low | low |
| **Hu 2009** | probably low | probably low | probably high | low | probably low | probably low | probably high |
| **Keh 2016** | low | low | low | low | low | low | low |
| **Liu 2012** | low | probably low | probably low | probably low | probably low | probably low | probably low |
| **Luce 1988** | low | low | low | probably high | probably low | low | probably high |
| **Lv 2017** | low | high | low | low | low | low | high |
| **Meduri 2007** | low | low | probably low | low | probably low | low | probably low |
| **Meduri 2009** | low | low | low | low | low | low | low |
| **Meijvis 2011** | low | low | low | low | low | low | low |
| **Menon 2017** | low | low | low | low | low | low | low |
| **Mirea 2014** | probably high | probably high | probably high | probably high | high | probably high | high |
| **Oppert 2005** | probably low | probably low | probably low | probably high | probably low | low | probably high |
| **Rezk 2003** | probably high | probably high | high | low | probably high | low | high |
| **Rianldi 2006** | probably low | probably high | high | low | low | low | high |
| **Sabry 2011** | probably low | probably high | probably low | low | low | low | probably high |
| **Schumer 1976** | probably low | high | probably low | low | low | low | high |
| **Slusher 1996** | probably high | probably high | probably low | low | low | low | probably high |
| **Snijders 2010** | low | low | probably low | low | low | low | probably low |
| **Sprung 1984** | probably high | probably high | high | low | low | low | high |
| **Sprung 2008** | low | low | low | low | low | low | low |
| **Tandan 2005** | low | low | low | probably high | probably high | probably low | probably high |
| **Tongyoo 2016** | low | low | low | low | low | low | low |
| **Torres 2015** | low | low | low | low | low | low | low |
| **Valoor 2009** | low | probably low | high | low | low | high | probably high |
| **VASSCSG 1987** | probably low | probably low | probably low | low | low | low | probably low |
| **Venkatesh 2017** | low | low | low | low | low | low | low |
| **Yildiz 2002** | probably low | probably low | probably low | low | low | low | probably low |
| **Yildiz 2011** | probably low | probably low | probably low | low | low | low | probably low |

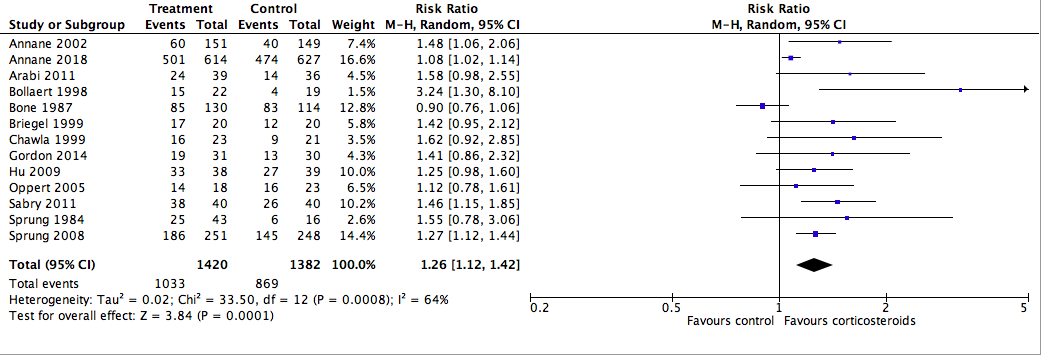
**3) Forest plot for ICU length of Stay**

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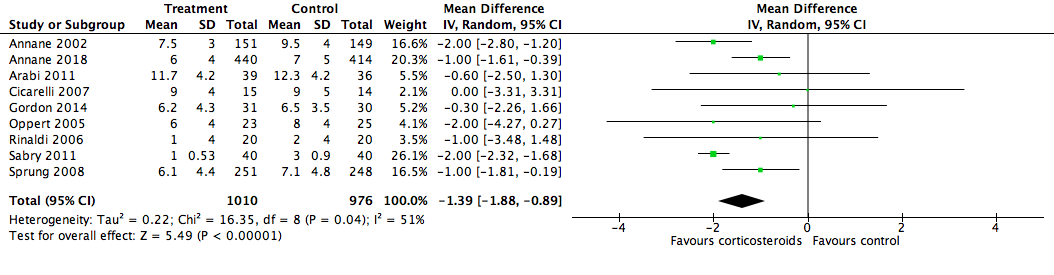
**4) Forest plot for hospital length of stay**

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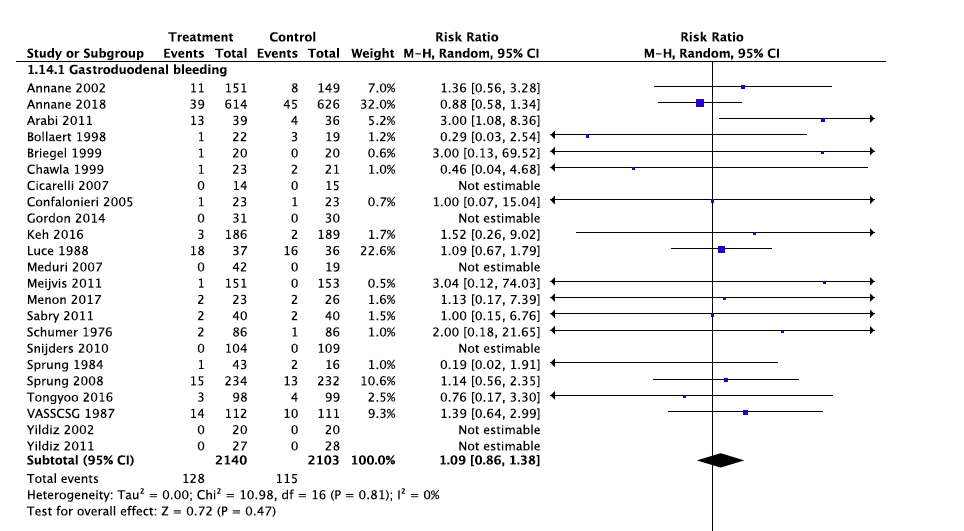
**5) Forest plot for shock reversal at day 7**

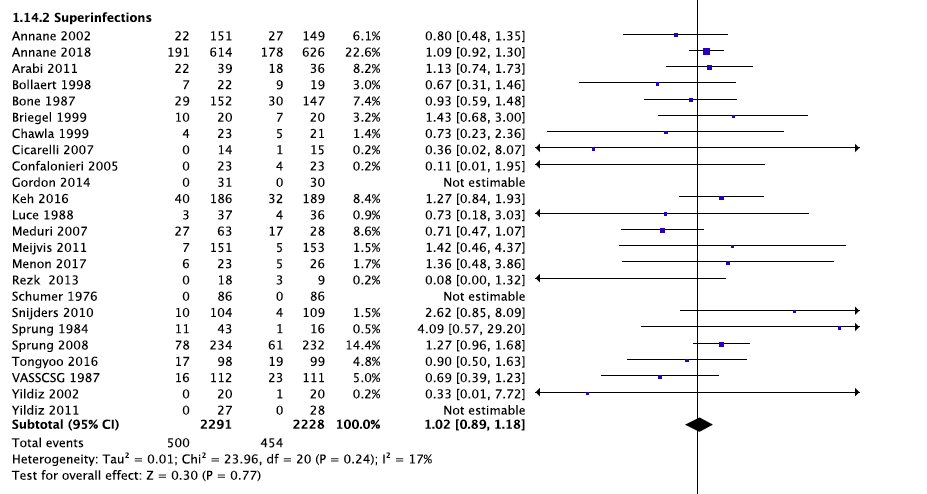
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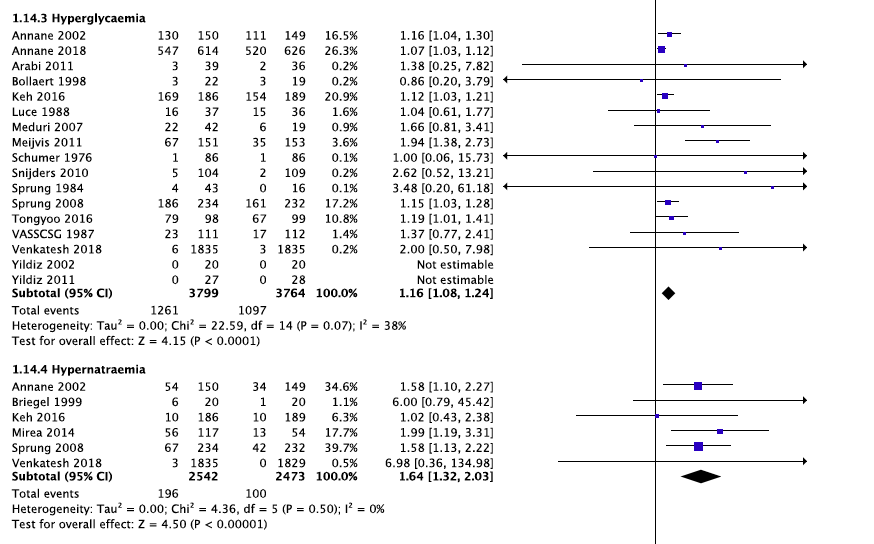
**6) Forest plot for SOFA score at day 7**

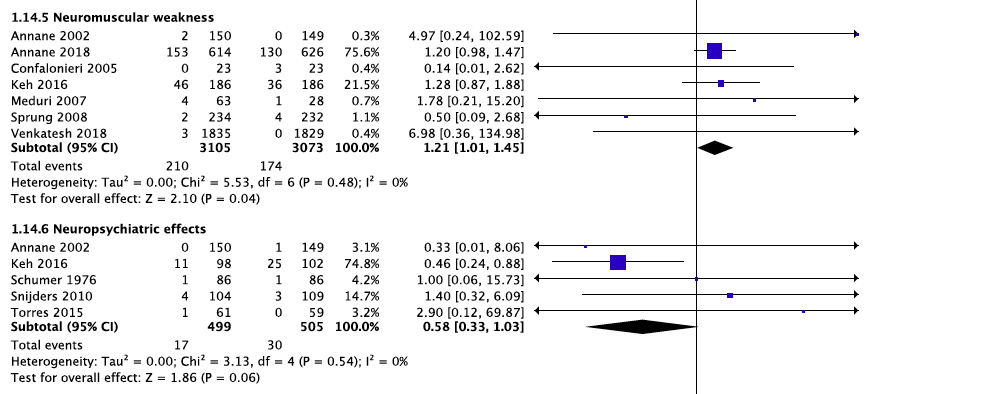
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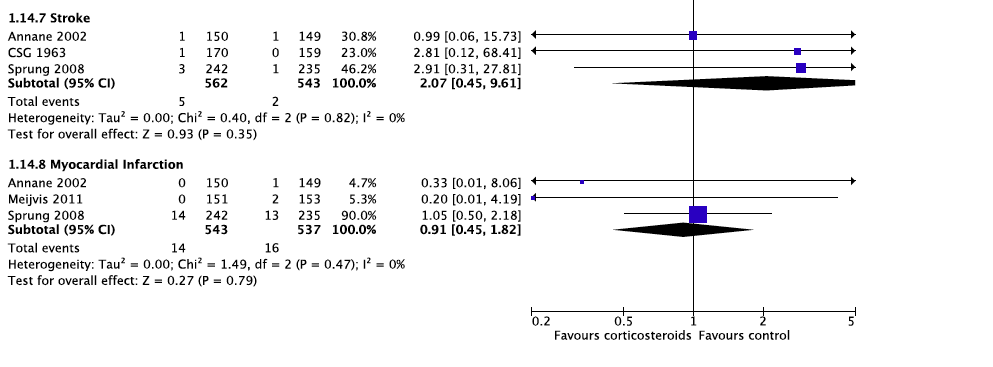
**7) Forest plot for adverse events**

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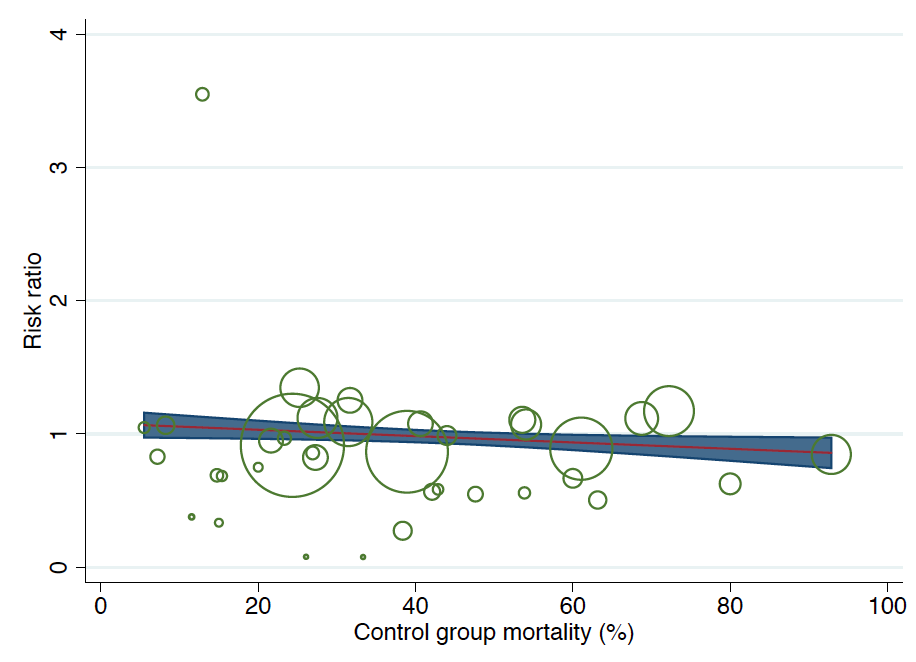
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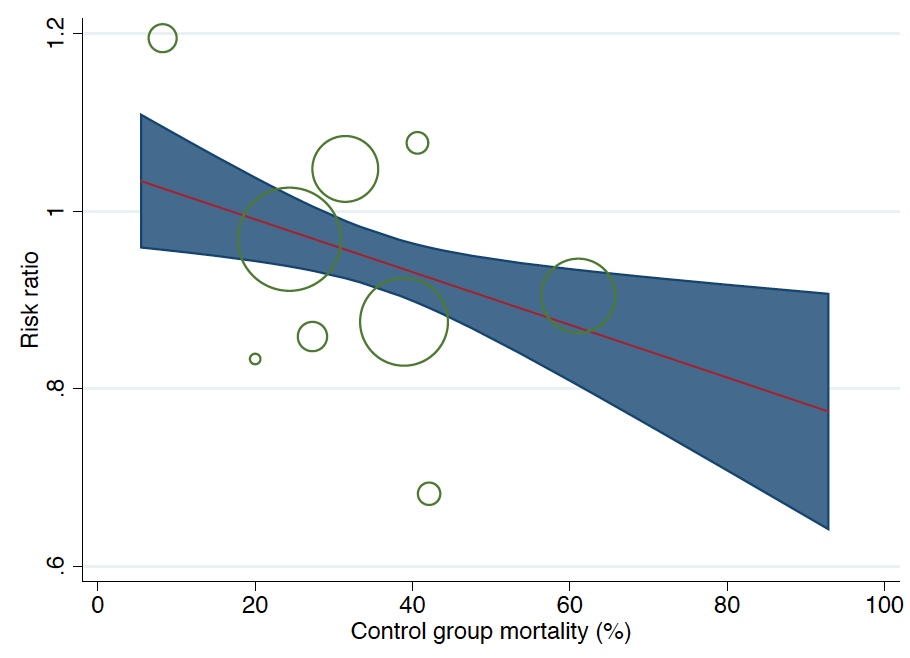
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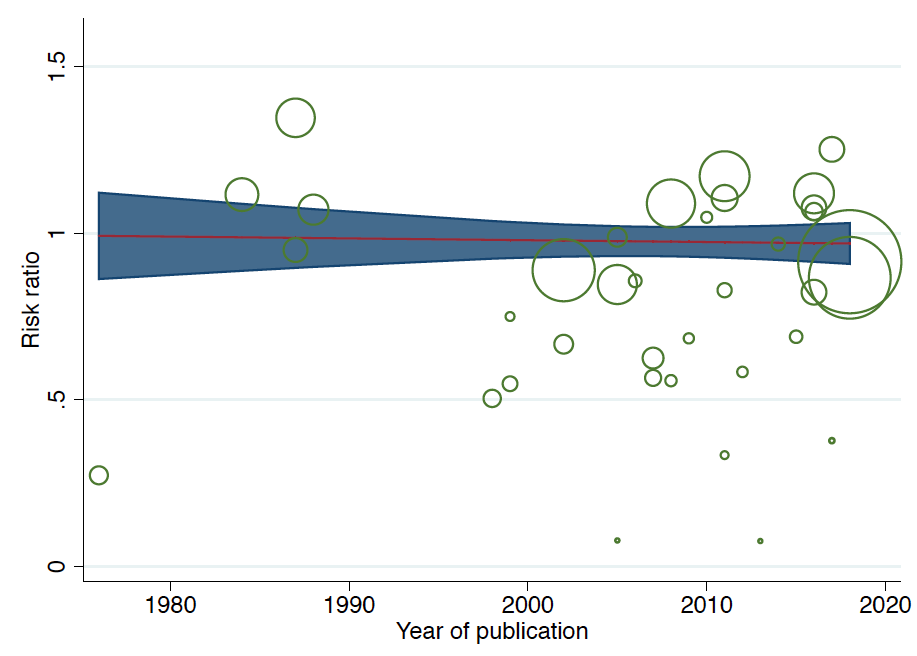
**8) Meta-regression for short-term mortality by control group mortality**

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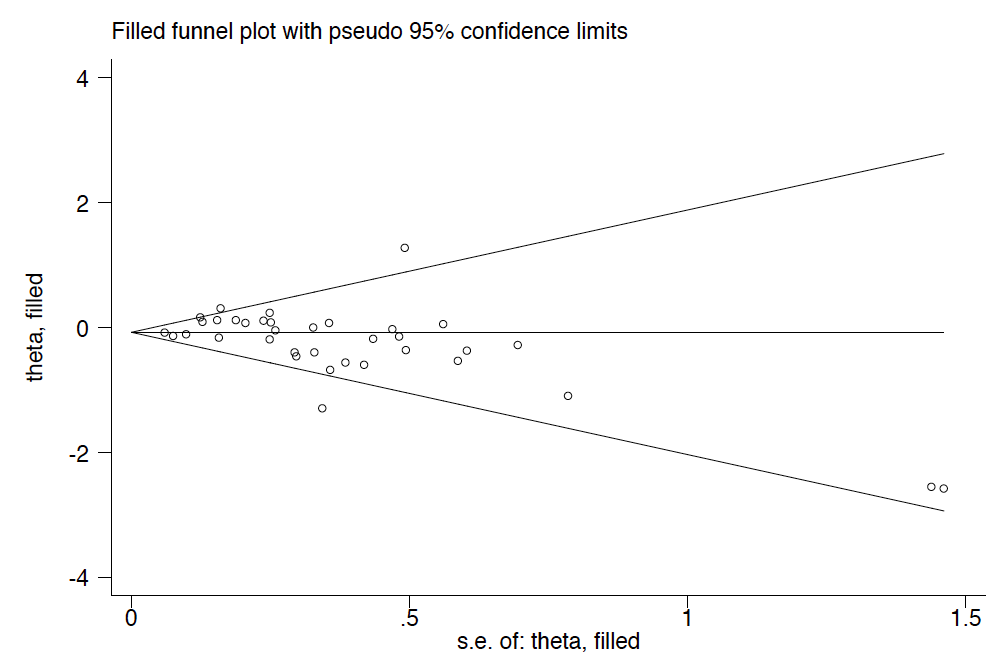
**9) Meta-regression for long-term mortality outcome by control group mortality**

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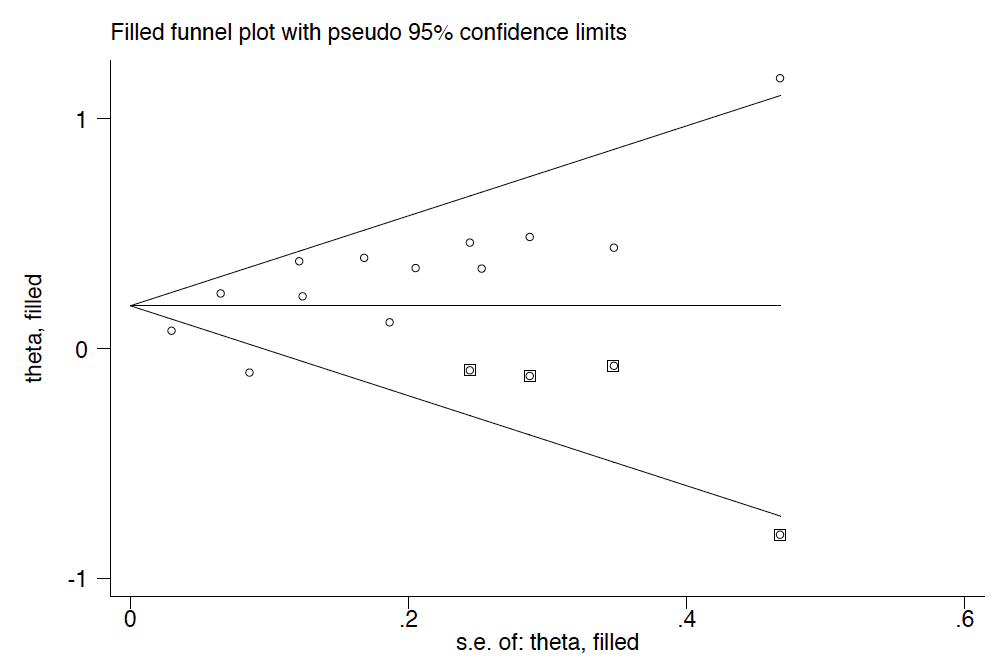
**10) Meta-regression for short-term mortality outcome by year of study publication**

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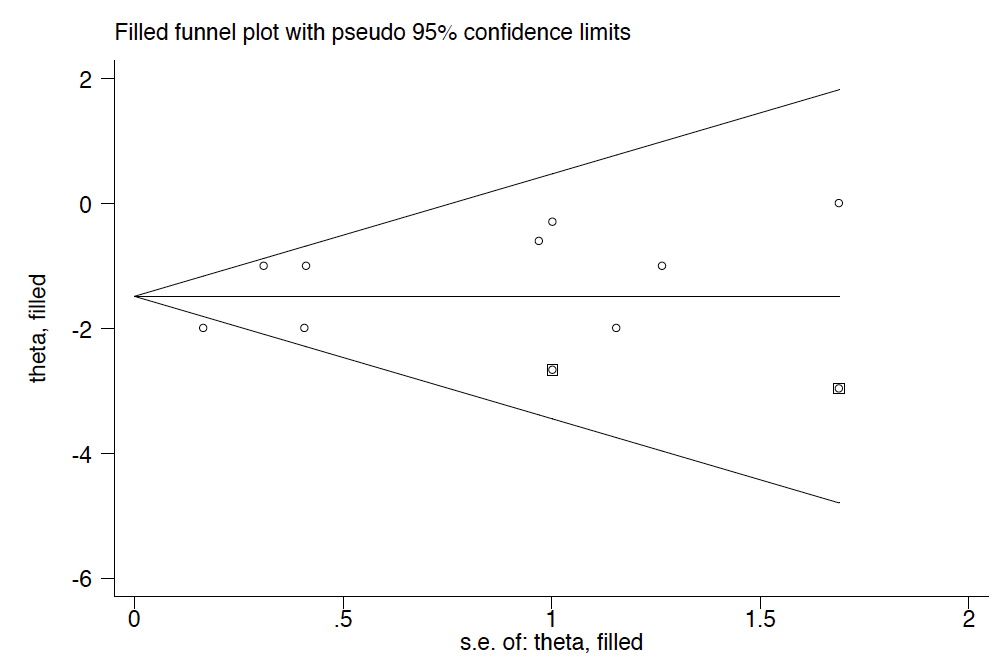
**11) Funnel plot for short-term mortality**

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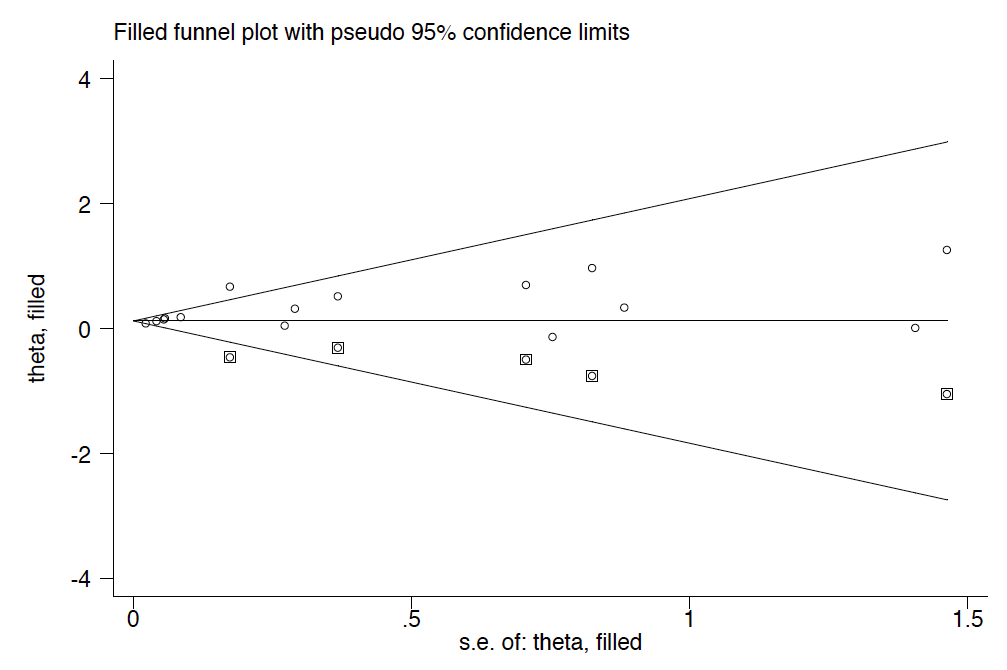
**12) Funnel plot for shock reversal at day 7**

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**13) Funnel plot for SOFA score at day 7**

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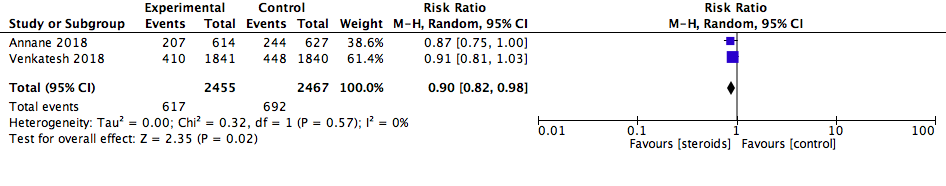
**14) Funnel plot for hyperglycemia**

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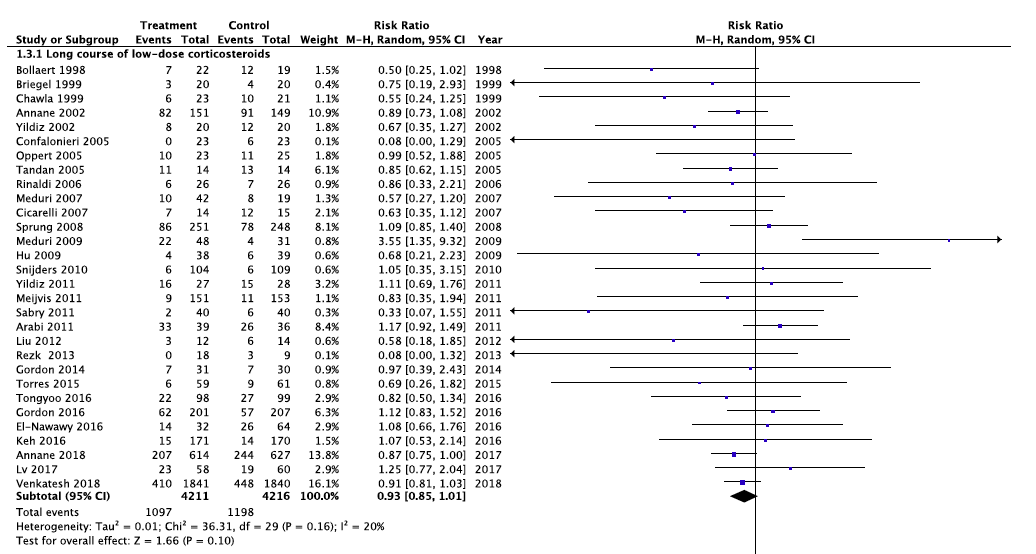
**15) Egger test p-values**

|  |  |
| --- | --- |
| **Outcome** | **Egger test p-value** |
| Short-term mortality | 0.111 |
| Long-term mortality | 0.940 |
| Shock Reversal at day 7 | 0.010 |
| SOFA score at day 7 | 0.082 |
| ICU Length of Stay | 0.554 |
| Hospital Length of Stay | 0.214 |
| Hyperglycemia | 0.013 |
| Superinfection | 0.166 |

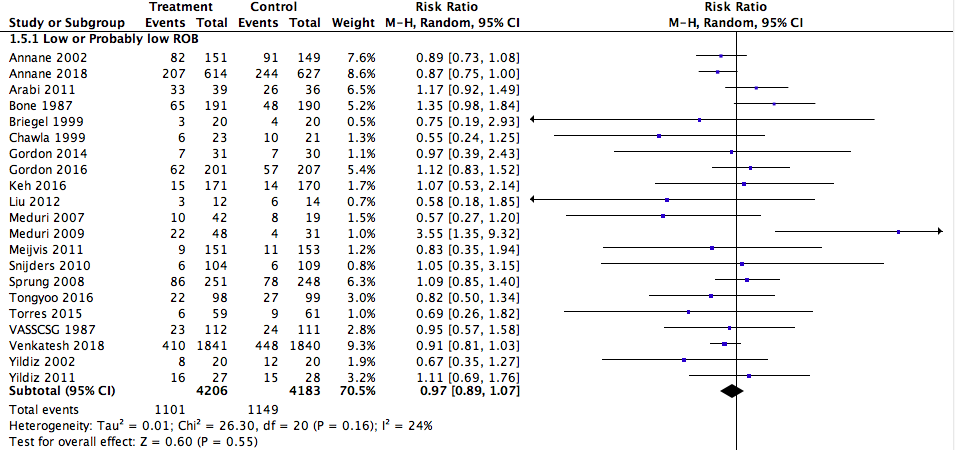
**16) Sensitivity analysis for short-term mortality – 2 most recent studies**

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**17) Sensitivity Analysis short-term mortality – excluding short course and high dose corticosteroids**

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**18) Sensitivity analysis for short-term mortality – excluding high risk or probably high risk of bias studies**

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**19) Meta-regression results (p-value for interaction) for subgroup analysis.**

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **RoB** | **Control Group mort** | **Sepsis w/o shock vs all others** | **Shock vs all others** | **ARDS vs all others** | **CAP vs all others** | **Sepsis vs shock** | **ARDS vs shock** | **CAP vs shock** | **Pulm vs non-pulm** | **Duration/Dose** | **HC vs all others** | **HC+FC vs all others** | **MP vs all others** |
| **Short-term Mortality** | 0.336 | 0.262 | 0.070 | 0.556 | 0.203 | 0.427 | 0.102 | 0.249 | 0.474 | 0.130 | 0.219 | 0.344 | 0.183 | 0.638 |
| **Long-term mortality** | N/A | 0.188 | 0.189 | 0.972 | 0.294 | N/A | 0.202 | 0.315 | N/A | 0.294 | N/A | 0.063 | 0.183 | 0.274 |
| **SOFA on day 7** | 0.104 | 0.617 | 0.754 | 0.099 | N/A | 0.087 | 0.865 | N/A | 0.087 | 0.087 | N/A | 0.988 | 0.780 | N/A |
| **Shock reversal at day 7** | 0.320 | 0.085 | N/A | 0.302 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | 0.098 | 0.564 | 0.150 |
| **Length of ICU Stay** | 0.600 | 0.248 | 0.800 | 0.190 | N/A | 0.255 | 0.661 | N/A | 0.233 | 0.128 | N/A | 0.700 | 0.588 | 0.912 |
| **Length of Hospital Stay** | 0.686 | 0.922 | 0.054 | 0.496 | N/A | 0.610 | 0.150 | N/A | 0.995 | 0.491 | N/A | 0.269 | 0.732 | 0.331 |
| **Superinfection** | 0.871 | 0.492 | 0.644 | 0.488 | 0.200 | 0.803 | 0.856 | 0.219 | 0.764 | 0.187 | 0.699 | 0.378 | 0.451 | 0.785 |
| **Hyperglycemia** | 0.594 | 0.201 | 0.414 | 0.251 | 0.884 | <0.001 | 0.899 | 0.267 | <0.001 | 0.018 | 0.922 | 0.313 | 0.271 | 0.416 |

RoB = risk of bias, mort = mortality, vs = versus, ARDS = acute respiratory distress syndrome, CAP = community acquired pneumonia, pulm = pulmonary, HC = hydrocortisone, FC = fludrocortisone, MP = methylprednisone, methylprednisolone or prednisone, SOFA = sequential organ failure assessment score, ICU = intensive care unit