DEPARTMENT OF EMERGENCY MEDICINE
MEDICAL UNIVERSITY OF VIENNA

CSM
CENTRE FOR STATISTICS IN MEDICINE

UNIVERSITY OF OXFORD

Influence of different mortality time points on pooled effect estimates

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Background

- Mortality reported as dichotomous outcome
- Arbitrarily defined time-points
- Is it appropriate to pool that?

Is it an issue?

Systematic review of all Crit Care RCTs 2000 to 2013, 50% sample

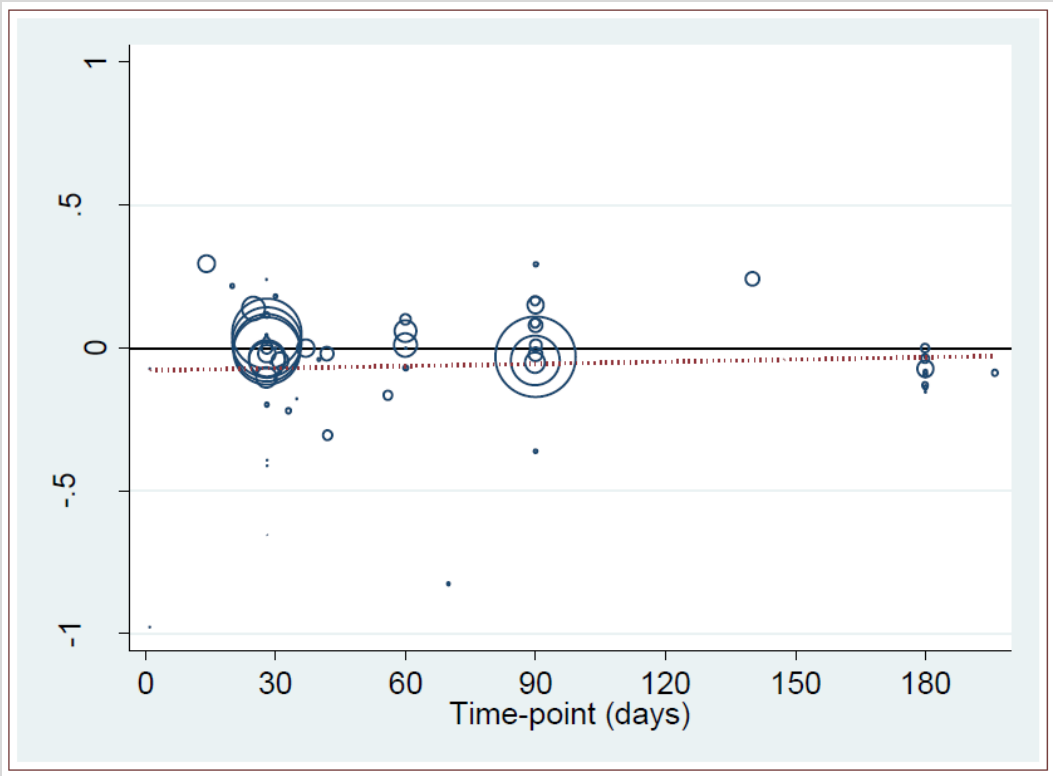
- In 106 studies 24 different time points reported
- Only one time point in 60 (57%) studies, two in 26 (25%), three in 14 (13%), four in 4 (4%), five in 2 (2%)
- Most frequent time points:
  - 28d (40%)
  - Hospital (35%)
  - ICU (27%)
  - 30d (13%)
  - 60d (6%)

Is it an issue?

All Cochrane systematic reviews on Crit Care (N=88)

- Time points reported similar to individual studies
- Strategies used in reviews to deal with different time points:
  - None stated: 50 (57%)
  - Separate: 9 (10%)
  - Use last: 9 (10%)
  - Defined time-point or closest to defined: 6 (7%)
  - Other: 6 (7%)

Does it matter?



Individual studies
Meta-regression:
No effect of time-point on
Δlog RR: Coeff. 0.00003
(95% CI -0.0005 to 0.0006)

Does it matter?

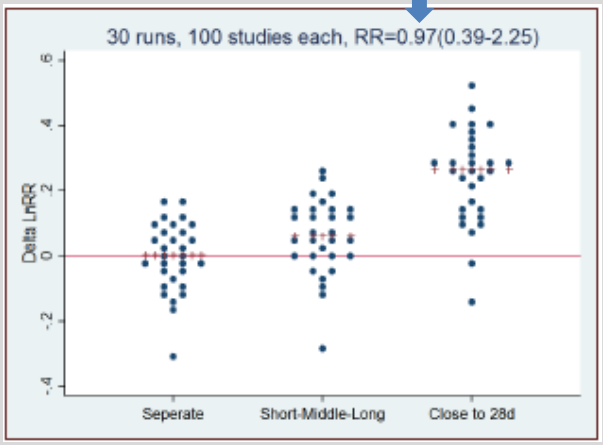
Recalculation of all 338 Cochrane meta-analyses

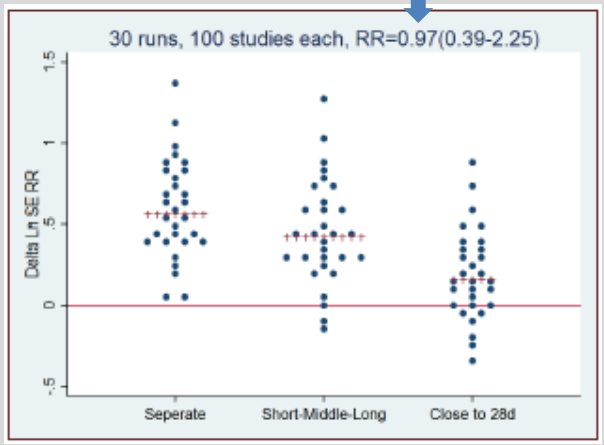
- Regression modelling to calculate the effect of pooling method on point-estimates, precision, significance
- No effect of method of pooling on Δlog RR
- Significant effects of separate on Δlog SE RR:
  Coeff. 1.13 (95% CI 0.86-1.40); p<0.001

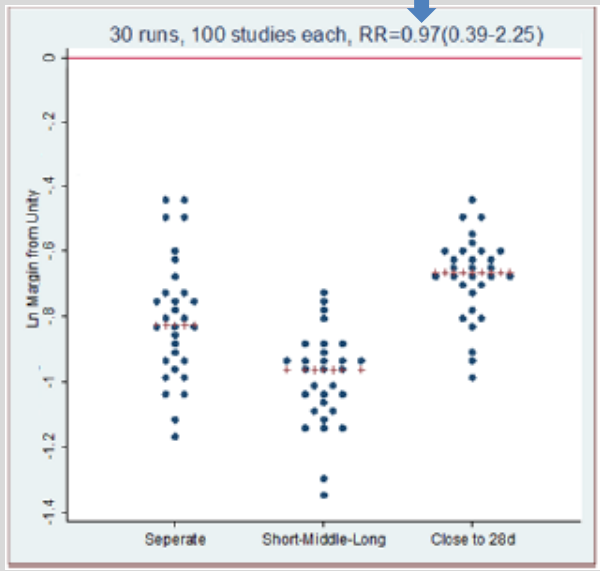
Simulation

- Generate random dataset based on structure of RCT dataset, vary magnitude and variability of effects
- Meta-analyses using different methods of pooling and regression modelling as before

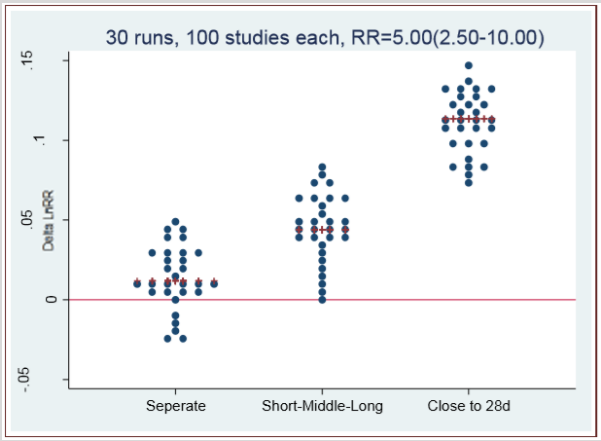
Simulation

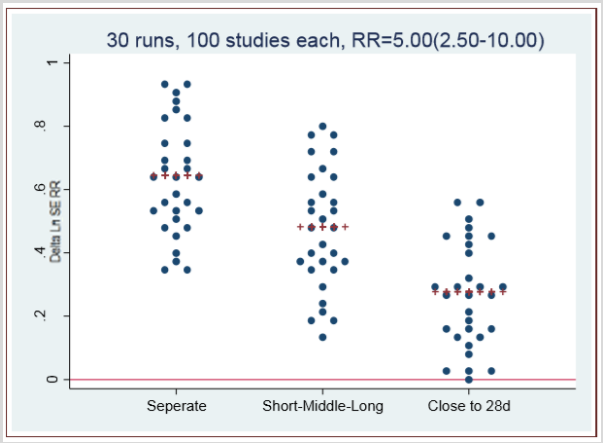

30 runs, 100 studies each, RR=0.97(0.39-2.25)
Delta LnRR
-.4
-.2
0
.2
.4
.6
Seperate
Short-Middle-Long
Close to 28d


30 runs, 100 studies each, RR=0.97(0.39-2.25)
Delta Ln SE RR
-.5
0
.5
1
1.5
Seperate
Short-Middle-Long
Close to 28d

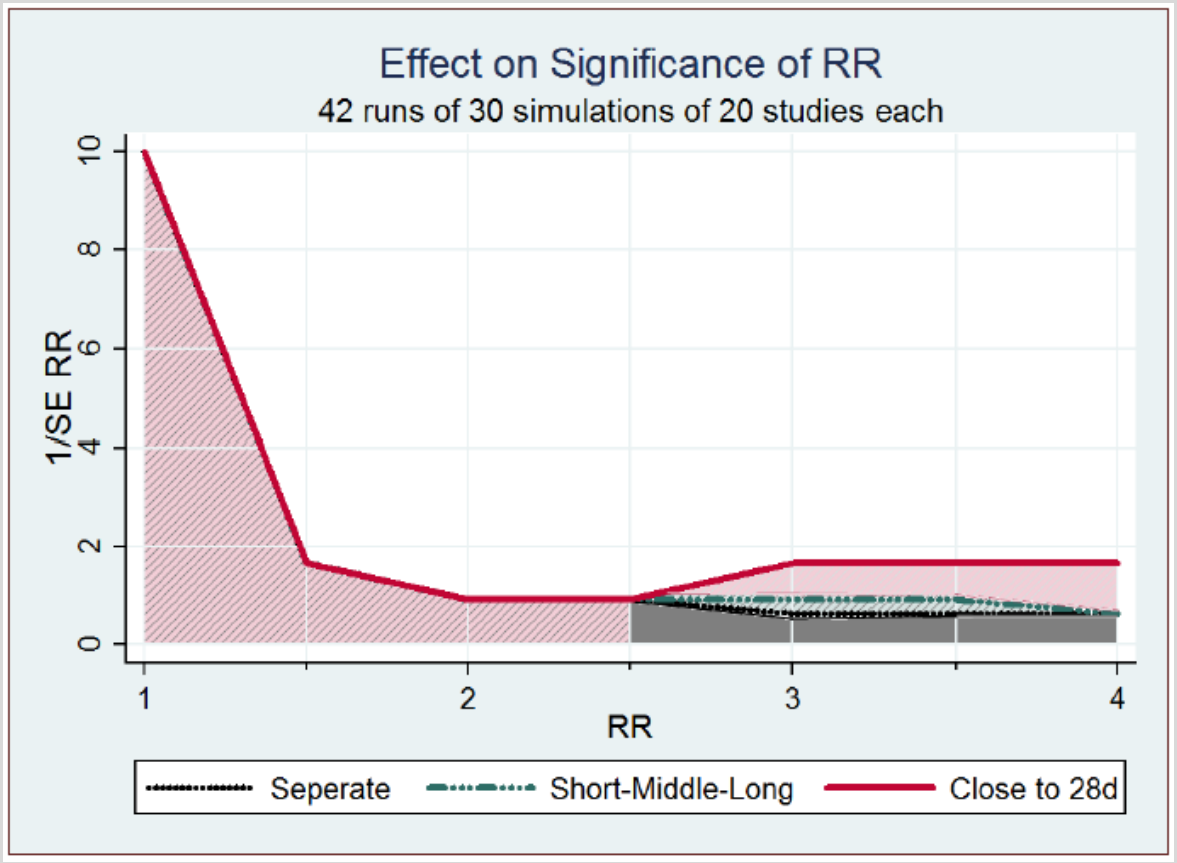

30 runs, 100 studies each, RR=0.97(0.39-2.25)
Ln Margin from Unity
0
-.2
-.4
-.6
-.8
-1
-1.2
-1.4
Seperate
Short-Middle-Long
Close to 28d

Simulation


30 runs, 100 studies each, RR=5.00(2.50-10.00)
Delta LnRR
-.05
0
.05
.1
.15
Seperate
Short-Middle-Long
Close to 28d


30 runs, 100 studies each, RR=5.00(2.50-10.00)
Delta Ln SE RR
0
.2
.4
.6
.8
1
Seperate
Short-Middle-Long
Close to 28d

Simulation


Effect on Significance of RR
42 runs of 30 simulations of 20 studies each
1/SE RR
0
2
4
6
8
10
1
2
3
4
RR
Seperate
Short-Middle-Long
Close to 28d

Conclusion

- Pooling mortality-data from different time points had no relevant influence on pooled point-estimates
- Limiting meta-analysis to only specific time points or performing separate analyses reduces precision of estimates, limits chance for significant findings
- **Use all available mortality data!**

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"In the long run we are all dead."

John Maynard Keynes, 1st Baron Keynes
A Tract on Monetary Reform.
Macmillan and Co. 1923. p. 80