Meta-analysis of rare (binary) events

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Question 3

An important application of meta-analysis is the integration of data for the purposes of evaluating drug safety. In this situation however, there may only be a few or even no events observed on one or more treatment arms in some or all of the studies. This seems an opportunity for the use of Bayesian methods, where prior distributions can be used in place of the “missing” data. What are the views of the panel on the use of Bayesian methods in this situation in particular and also more generally when integrating efficacy data?

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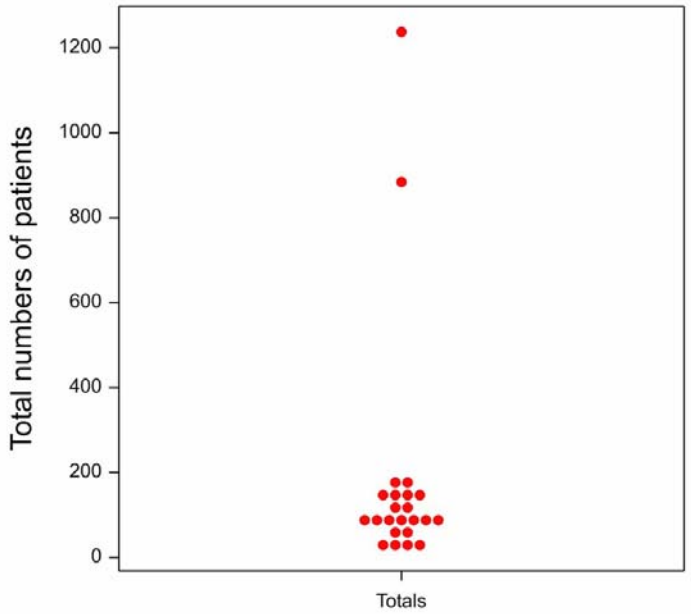
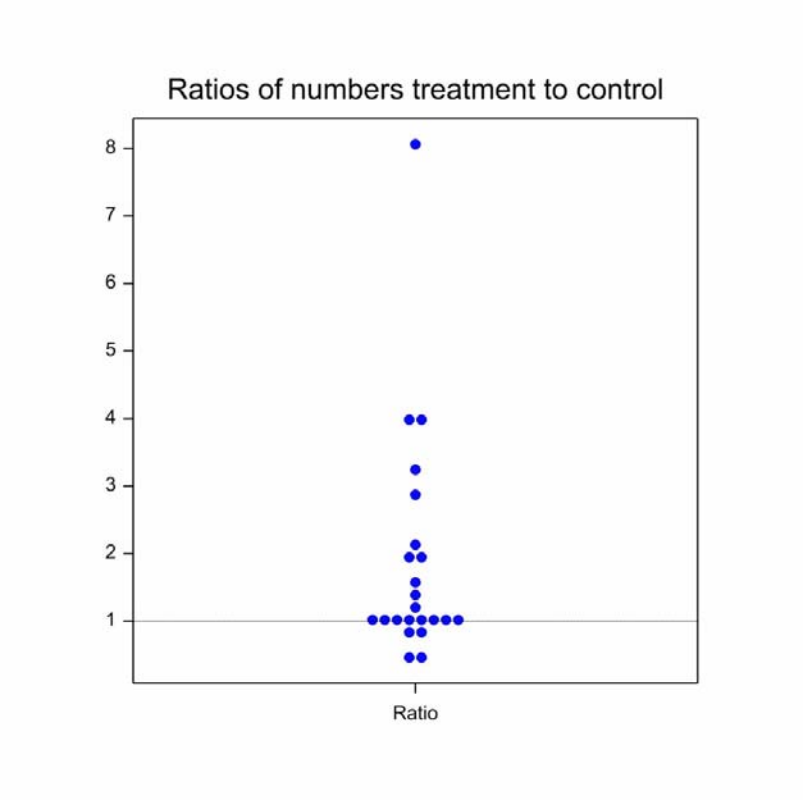
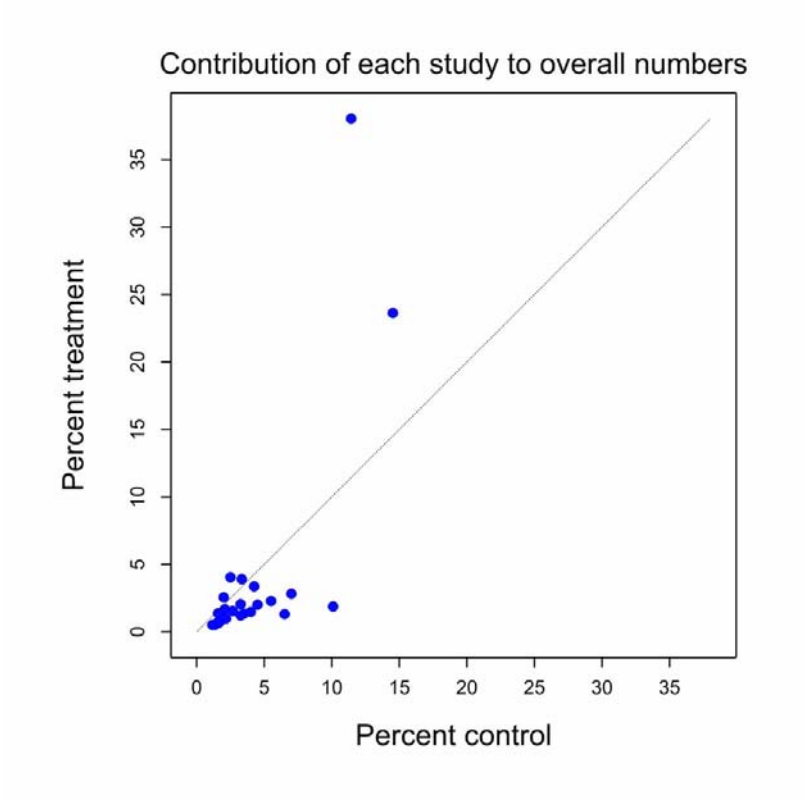
An example

- Meta-analysis of 23 trials of HRT
- CV events
- Quoted in Sweeting et al (2004)
- Events very rare
  - 17 Events among 4164 patients
- Trials of very differing sizes
- Arms very unbalanced
- Many empty cells
  - 36 empty out of 46
  - 16 trials out of 23 no events



Treatment given is strongly confounded with study



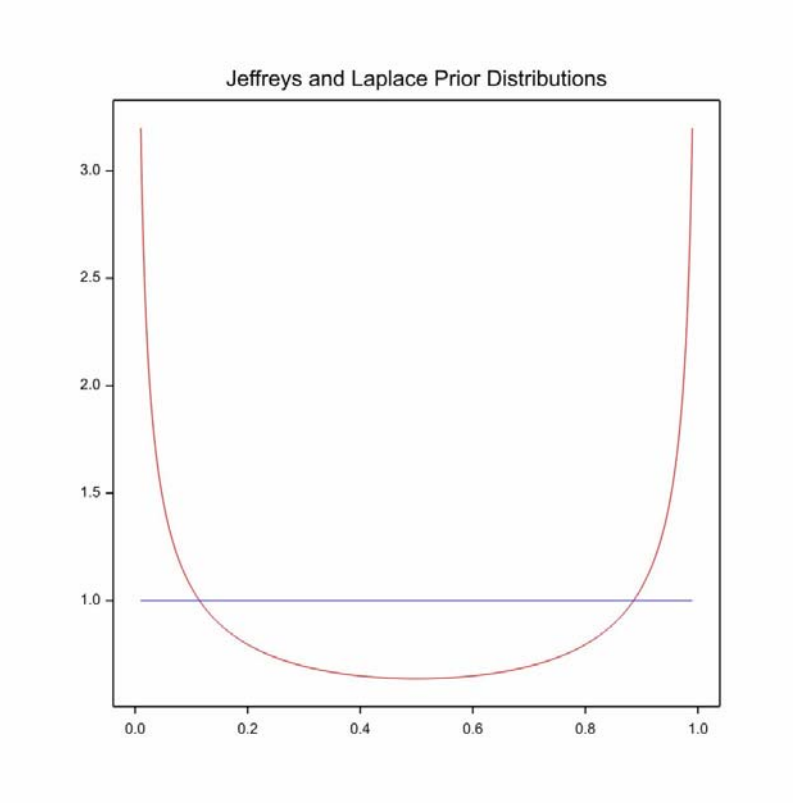


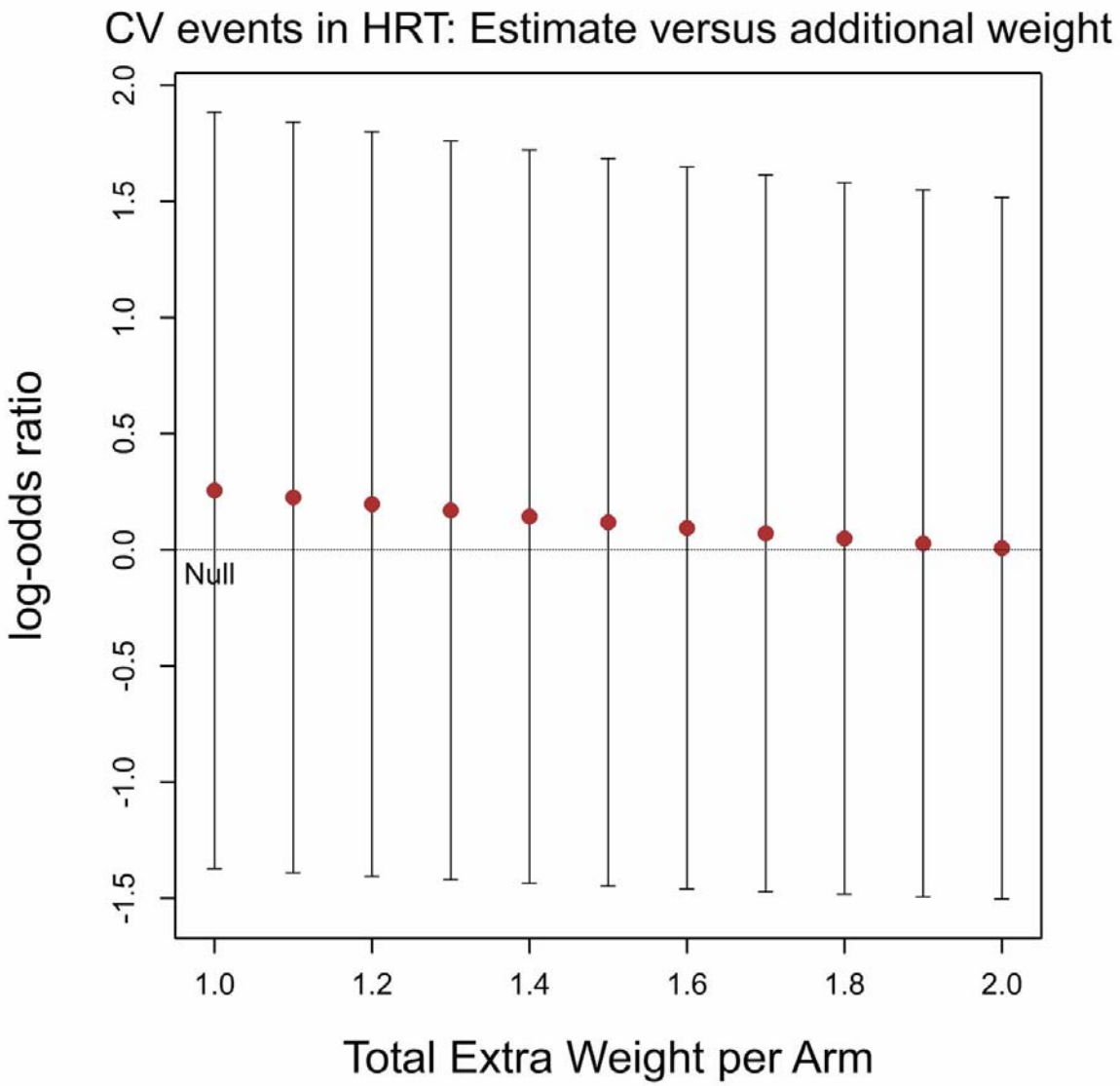
Issues

- Log-odds scale generally better than risk difference (less heterogeneity) but provides estimation problems for low numbers
- If we have random main effect of trial we have recovery of inter-trial information
  - Concurrent control abandoned
- Adding ½ to each cell?
  - Biasing because of unequal allocation ratios
  - Over-states information available
  - It's like adding your prior several times

Recommendations

- When designing your programme, don't ever use unequal allocation if you are not prepared to be fully Bayesian
- Allocate a total of somewhere between 2 and 4 observations proportionately to cells *on an independence model*
  - Proportionate to numbers on trial and overall in arm
  - 1 (Jeffreys) to 2 (Laplace) per arm
- Consider expected rather than empirical weights
- ?????




CV events in HRT: Estimate versus additional weight
log-odds ratio
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
Null
1.0
1.2
1.4
1.6
1.8
2.0
Total Extra Weight per Arm