Conditional power computations applied to data prior to CRASH trial
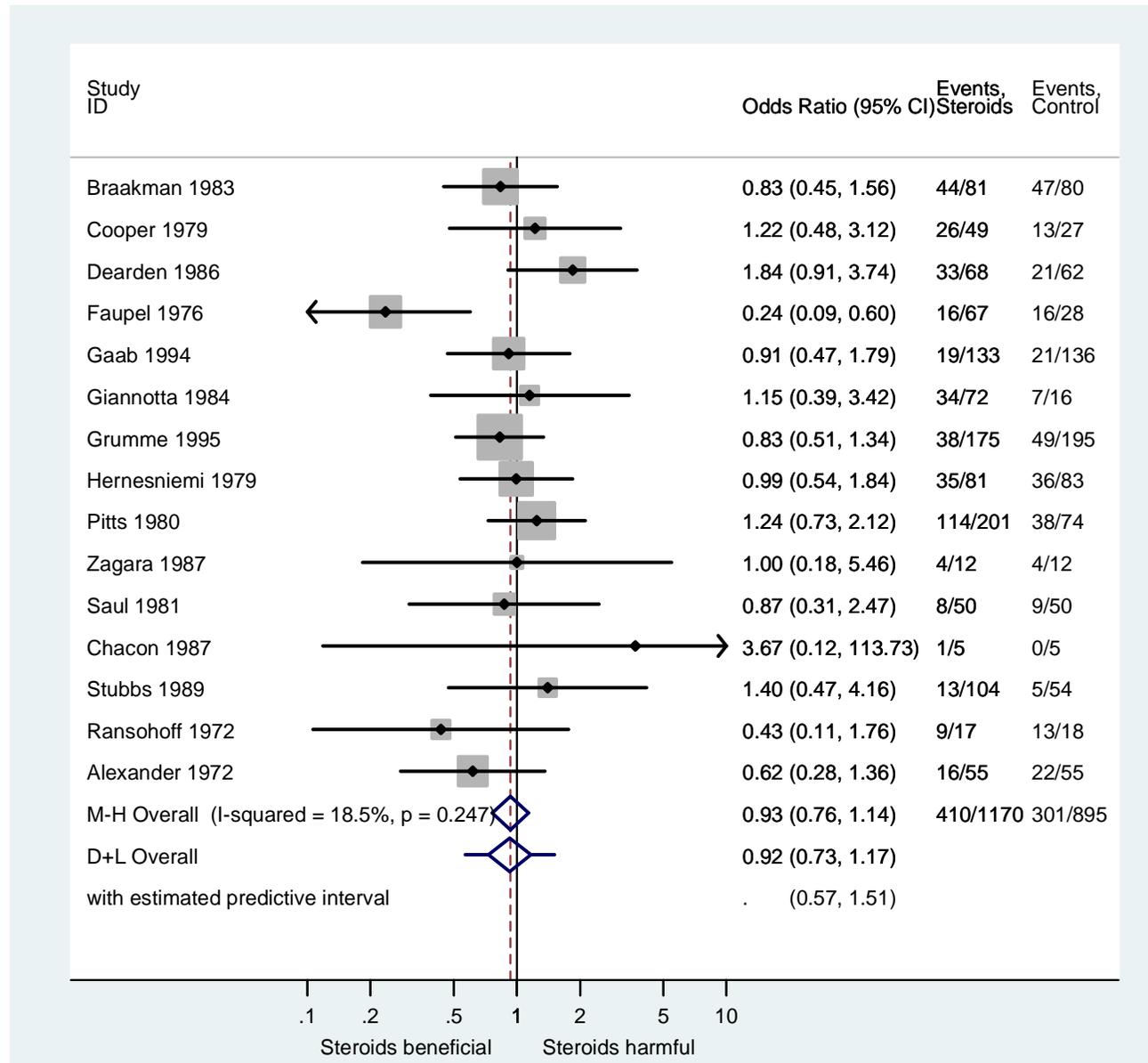
Julian Higgins, University of Bristol

Planning future studies based on the conditional power of a meta-analysis

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Systematic reviews often provide recommendations for further research. When meta-analyses are inconclusive, such recommendations typically argue for further studies to be conducted. However, the nature and amount of future research should depend on the nature and amount of the existing research. We propose a method based on conditional power to make these recommendations more specific. Assuming a random-effects meta-analysis model, we evaluate the influence of the number of additional studies, of their information sizes and of the heterogeneity anticipated among them on the ability of an updated meta-analysis to detect a prespecified effect size. The conditional powers of possible design alternatives can be summarized in a simple graph which can also be the basis for decision making. We use three examples from the *Cochrane Database of Systematic Reviews* to demonstrate our strategy. We demonstrate that if heterogeneity is anticipated, it might not be possible for a single study to reach the desirable power no matter how large it is. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: meta-analysis; power; sample size; evidence-based medicine; random effects; cumulative meta-analysis

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Statistical methods for using meta-analysis to plan future research

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What sample size would a new trial have to have to give the (post-CRASH) meta-analysis adequate power?

Study ID	Odds Ratio (95% CI)	Events, Steroids	Events, Control
Braakman 1983	0.83 (0.45, 1.56)	44/81	47/80
Cooper 1979	1.22 (0.48, 3.12)	26/49	13/27
Dearden 1986	1.84 (0.91, 3.74)	33/68	21/62
Faupel 1976	0.24 (0.09, 0.60)	16/67	16/28
Gaab 1994	0.91 (0.47, 1.79)	19/133	21/136
Giannotta 1984	1.15 (0.39, 3.42)	34/72	7/16
Grumme 1995	0.83 (0.51, 1.34)	38/175	49/195
Hernesniemi 1979	0.99 (0.54, 1.84)	35/81	36/83
Pitts 1980	1.24 (0.73, 2.12)	114/201	38/74
Zagara 1987	1.00 (0.18, 5.46)	4/12	4/12
Saul 1981	0.87 (0.31, 2.47)	8/50	9/50
Chacon 1987	3.67 (0.12, 113.73)	1/5	0/5
Stubbs 1989	1.40 (0.47, 4.16)	13/104	5/54
Ransohoff 1972	0.43 (0.11, 1.76)	9/17	13/18
Alexander 1972	0.62 (0.28, 1.36)	16/55	22/55
M-H Overall (I-squared = 18.5%, p = 0.247)	0.93 (0.76, 1.14)	410/1170	301/895
D+L Overall	0.92 (0.73, 1.17)		
with estimated predictive interval	. (0.57, 1.51)		

.1   .2   .5   1   2   5   10

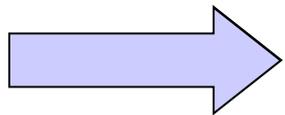Steroids beneficial   Steroids harmful

Power of a meta-analysis

- We can work out the power of a meta-analysis to detect an effect μ

$$\text{Power} = 1 - \Phi\left(c_\alpha - \frac{\mu}{\text{SE}(\mu)} \right) + \Phi\left(-c_\alpha - \frac{\mu}{\text{SE}(\mu)} \right)$$
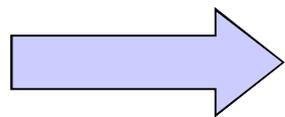
Power of existing data to detect OR = 0.9 (FE) is 18%
Power of existing data to detect OR = 0.8 (FE) is 58%

Power of existing data to detect OR = 0.9 (RE) is 14%
Power of existing data to detect OR = 0.8 (RE) is 47%

Hedges and Pigott.
Psychological Methods 2001; 6: 203–217

Conditional power of a meta-analysis

- For future studies, we derive power to detect overall mean effect μ given the result of the existing meta-analysis

- Suppose there are to be **m new studies**, each with (FE) **weight W/m**

$$\text{Power} = \Phi\left(-\sqrt{\frac{m + W\tau^2}{mW}}\left(c_\alpha\sqrt{\sum_{i=1}^{k} w_{i,old}^* + \frac{mW}{m + W\tau^2}} - \sum_{i=1}^{k} w_{i,old}^* y_{i,old}\right) + \frac{m\mu}{\sqrt{\frac{m^2}{W} + m\tau^2}}\right)$$

$$+ \Phi\left(-\sqrt{\frac{m + W\tau^2}{mW}}\left(c_\alpha\sqrt{\sum_{i=1}^{k} w_{i,old}^* + \frac{mW}{m + W\tau^2}} + \sum_{i=1}^{k} w_{i,old}^* y_{i,old}\right) - \frac{m\mu}{\sqrt{\frac{m^2}{W} + m\tau^2}}\right)$$

- We can partition heterogeneity τ^2 into 'old' and 'new' bits
 - or set it to 0 (for a fixed-effect analysis)

Conditional power of **fixed-effect** meta-analysis to detect a difference of **OR = 0.9** having observed a difference of OR = 0.93 [0.76; 1.14]
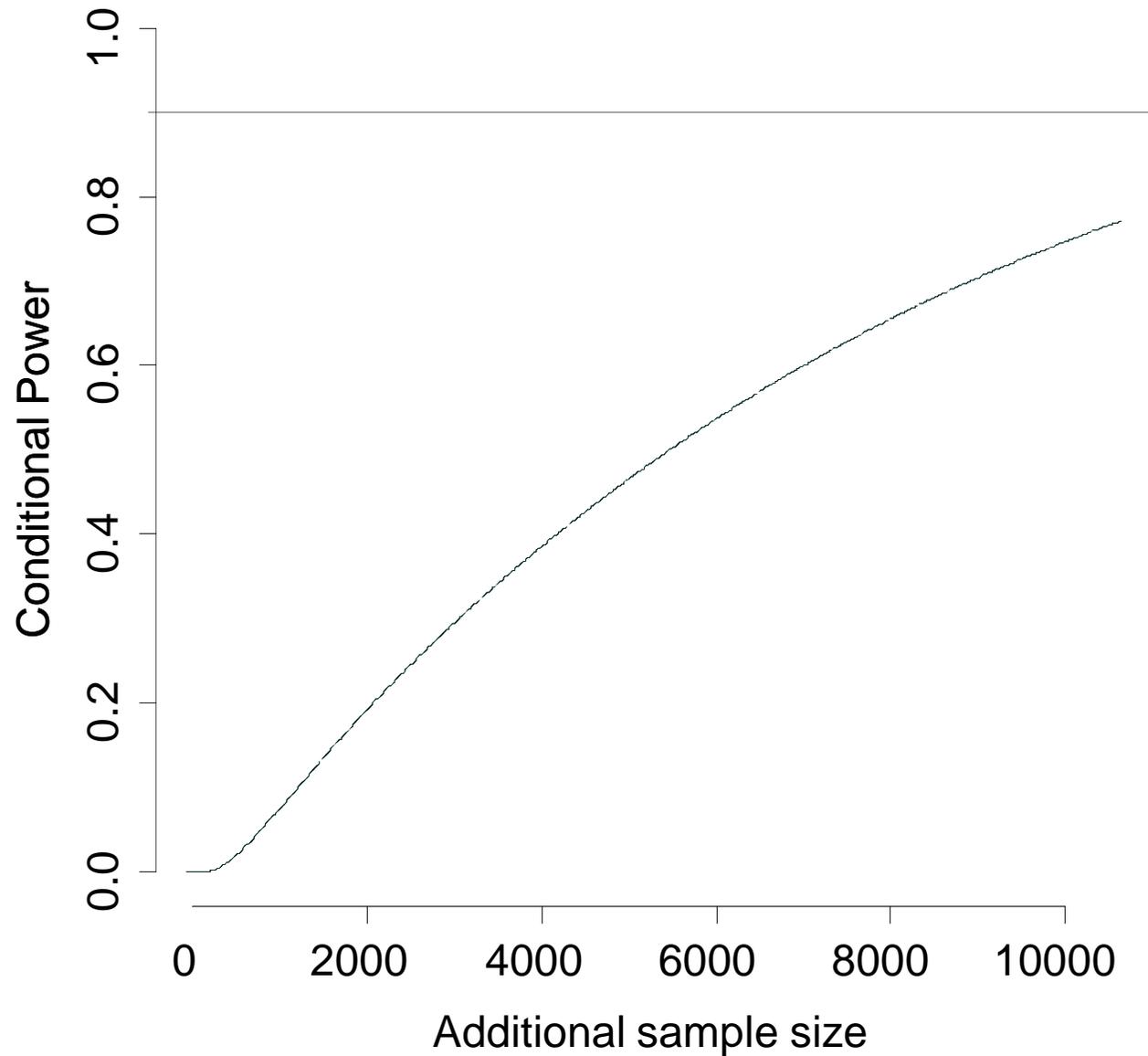
Conditional power of **random-effects** meta-analysis to detect a difference of **OR = 0.9** having observed a difference of OR = 0.92 [0.73; 1.17]
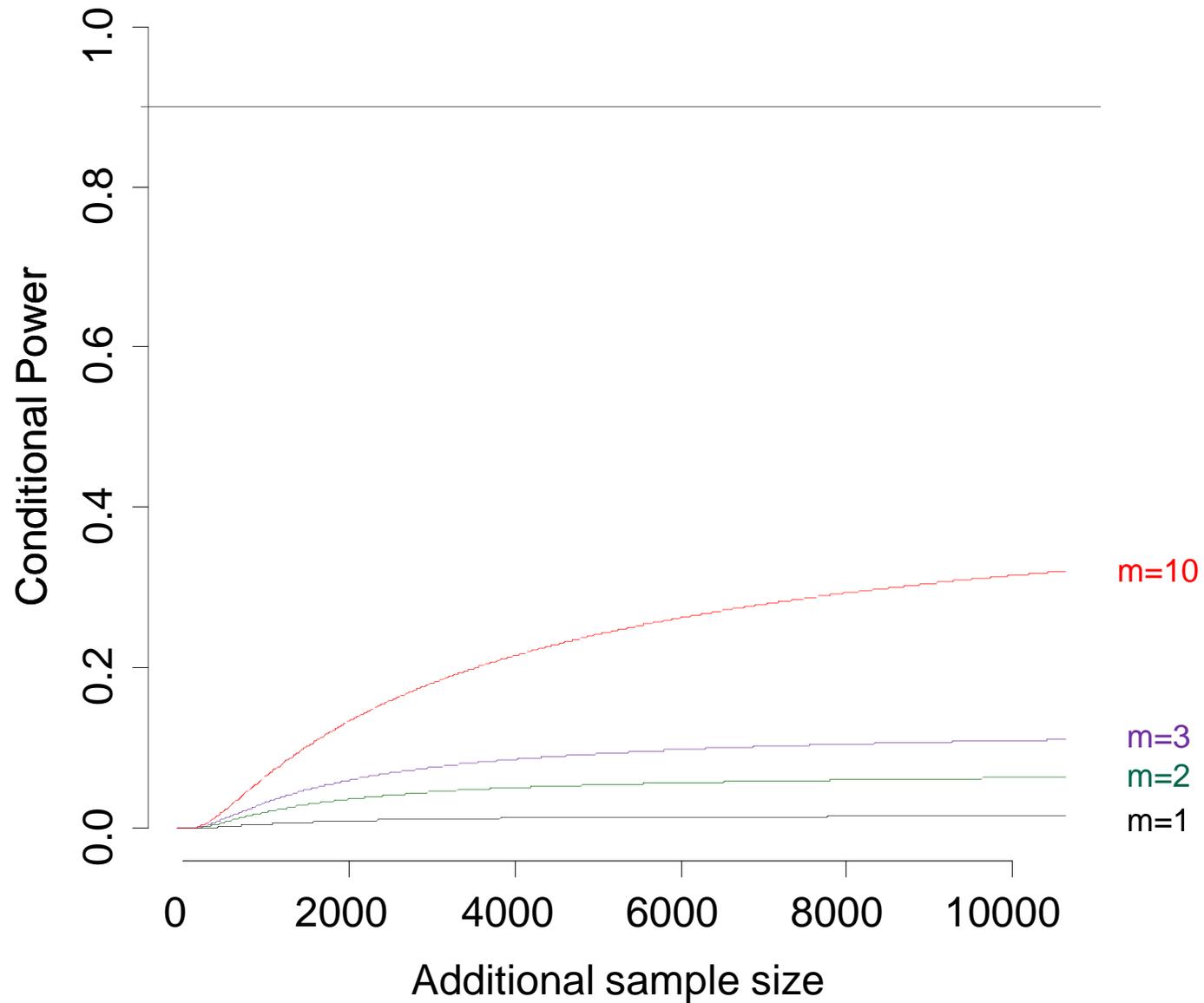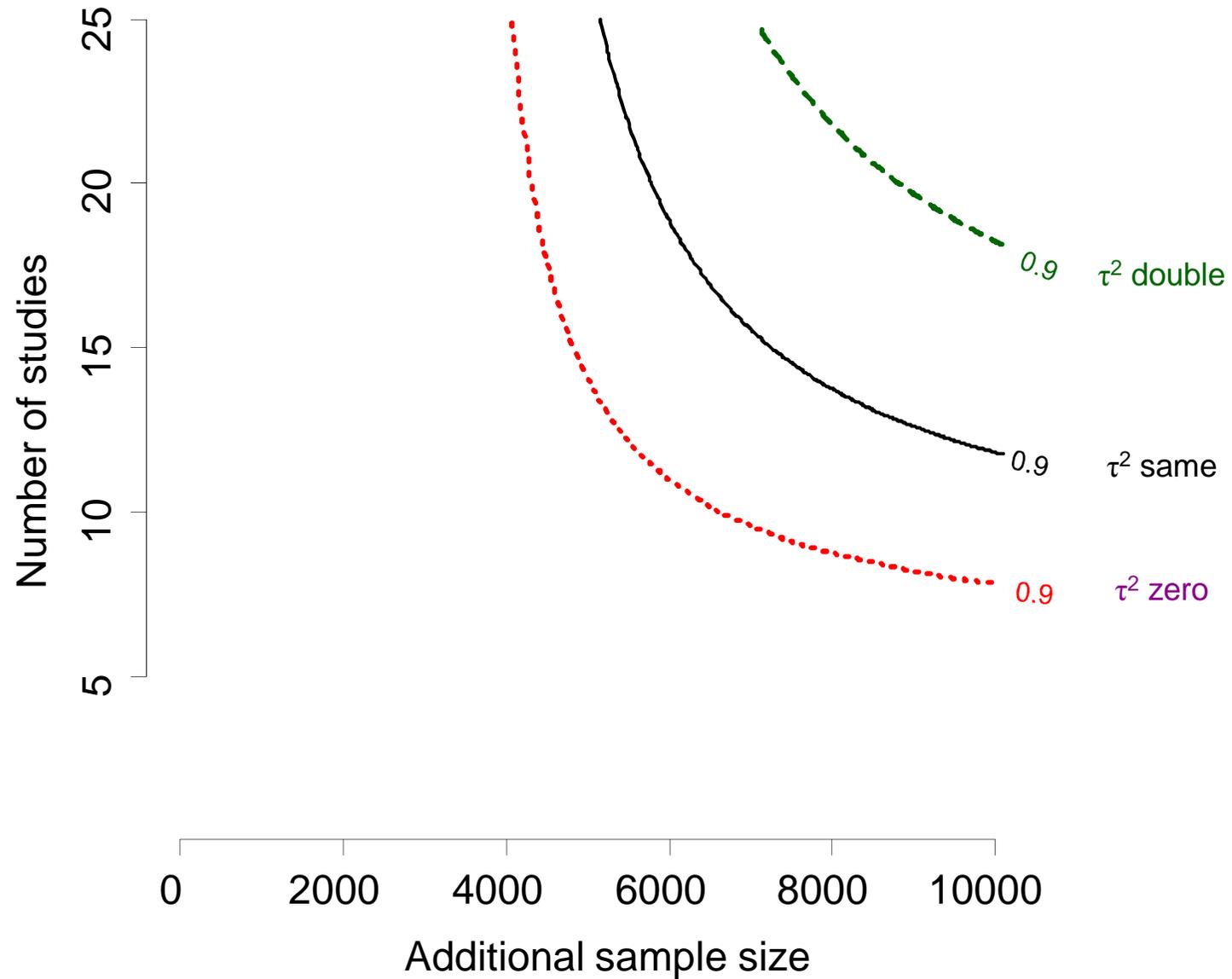
Conditional power of **fixed-effect** meta-analysis to detect a difference of **OR = 0.8** having observed a difference of OR = 0.93 [0.76; 1.14]
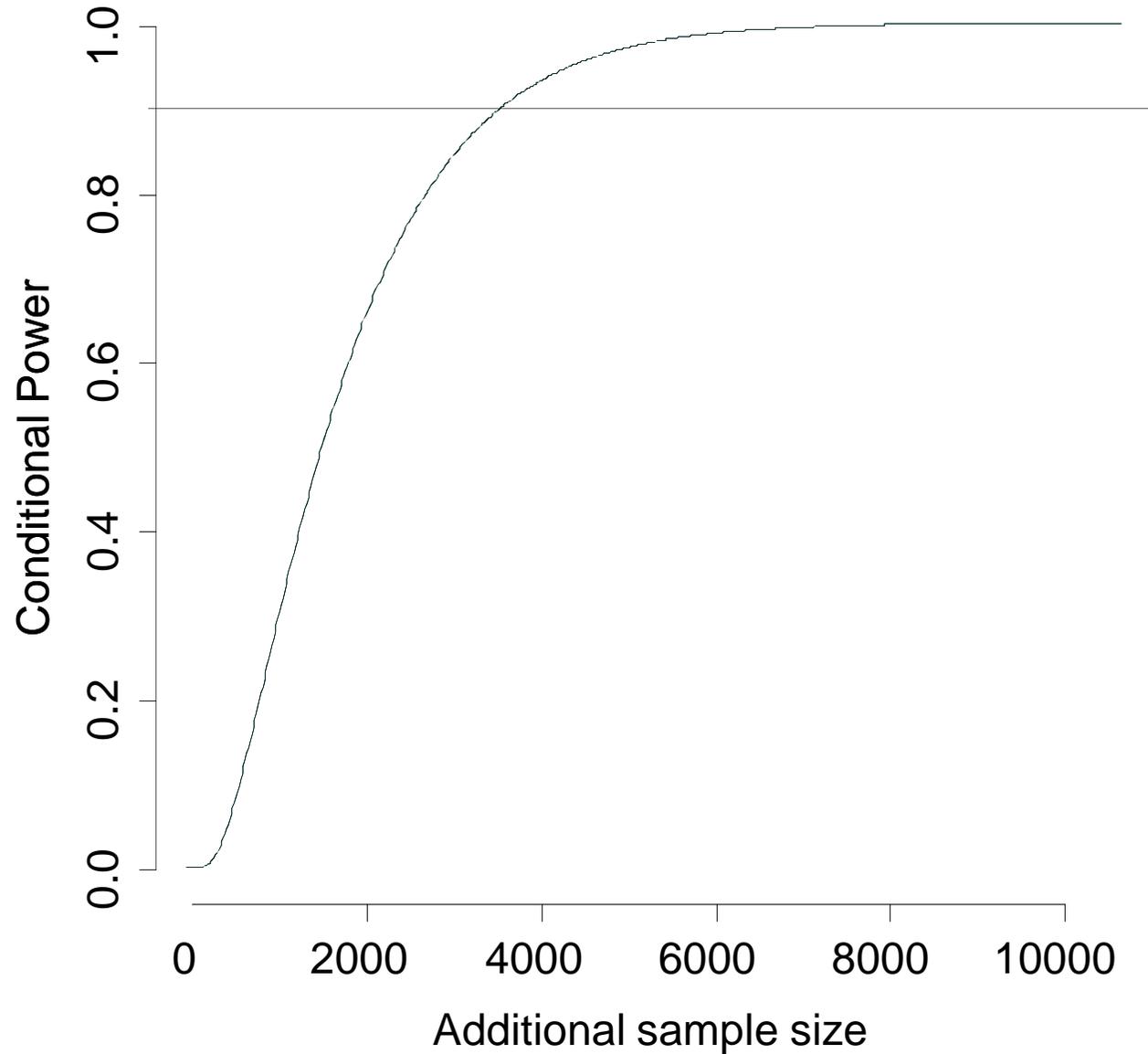
Conditional power of **random-effects** meta-analysis to detect a difference of **OR = 0.8** having observed a difference of OR = 0.92 [0.73; 1.17]
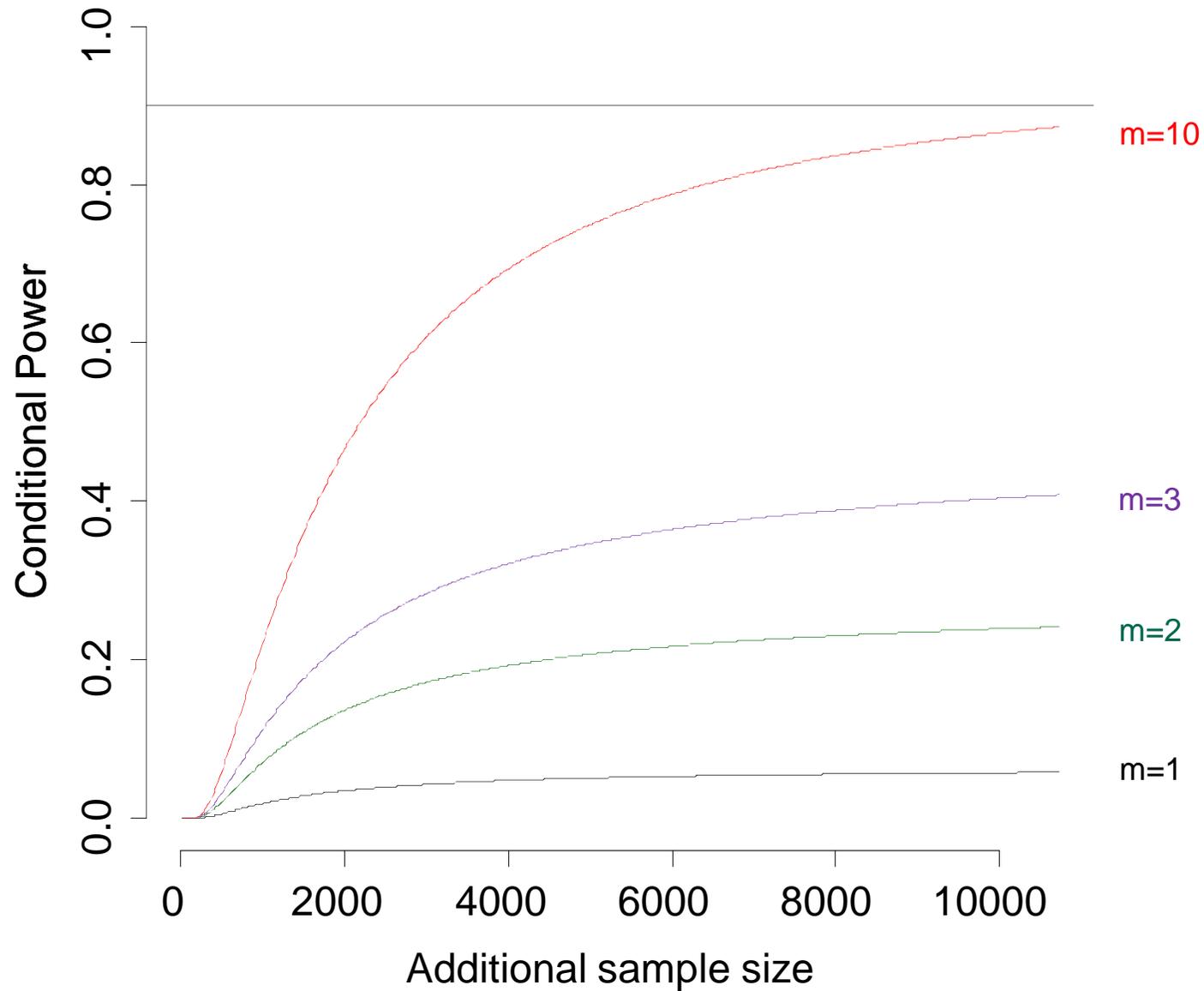
Contour lines for **90%** conditional power to detect OR = 0.8 having observed a difference of OR = 0.92 [0.73; 1.17]

Number of studies (y-axis): 5, 10, 15, 20, 25

Additional sample size (x-axis): 0, 2000, 4000, 6000, 8000, 10000

0.9 τ^2 double

0.9 τ^2 same

0.9 τ^2 zero

Contour lines for **80%** conditional power to detect OR = 0.8 having observed a difference of OR = 0.92 [0.73; 1.17]