reading key references

stats methodologists meeting

22 April 2015

Empirical Evidence of Bias

Dimensions of Methodological Quality associated with Estimates of Treatment Effects in Controlled Trials

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…inadequate approaches to controlled trials lead to inflated effect sizes

Design of Investigation

- 33 meta-analyses of 250 trials

- quality measures:
  - treatment allocation concealed? (Y/N/can't tell)
  - allocation sequence generated properly? (Y/N)
  - all randomised participants included? (Y/N)
  - double-blind? (Y/N)

- do the quality categories affect the effect-sizes?

Table 3.—Association Between Four Dimensions of Methodological Quality and Estimates of Treatment Effects in the 229 Adequately and Unclearly Concealed Trials*

Measure of Methodological Quality	Ratio of Odds Ratios (95% Confidence Interval)	χ^2 (df)	P
Allocation concealment			
Adequate	1.00 (referent)	32.9 (1)	<.001
Unclear	0.70 (0.62-0.79)		
Sequence generation			
Adequate	1.00 (referent)	0.31 (1)	.58
Inadequate	0.95 (0.81-1.12)		
Exclusions			
No	1.00 (referent)	0.99 (1)	.32
Yes	1.07 (0.94-1.21)		
Double-blinded			
Yes	1.00 (referent)	6.16 (1)	.01
No	0.83 (0.71-0.96)		

*Multiple logistic regression model with the dependent variable being binary outcome measures from each meta-analysis. The independent variables included a binary variable for treatment group (experimental vs control); indicator variables to control for the effects of each of the 229 trials; terms for the "meta-analysis by treatment group" interaction to control for the different summary odds ratios for the treatment effects in the 33 meta-analyses; and the four "quality measure by treatment" interaction terms displayed in this table to analyze their associations with estimates of treatment effects. Model deviance=325.3; df=192.

Analysis

- Data: 33 meta-analyses
  - 229 trials (treatment v control, binary outcome)

- Model (logistic regression):
  - trials (229df including overall mean)
  - treatments (33df => 196df 'residual' from 'base')
  - add terms for: allocation concealment, sequence generation, exclusions, double-blinded (4df)

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Model deviance=325.3; df=192.

(estimated scale parameter ≈ 1.7)

In separate models not shown, we used an adjustment to the scale parameter to take rough account of overdispersion (extrabinomial variation) in estimating SEs[24] for the effects of inadequately and unclearly concealed trials. While yielding wider confidence intervals (CIs),[23] our basic conclusions remained unchanged.

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Examining 33 separate logistic regression analyses, the estimates of treatment effects for the unclearly concealed trials were larger (exaggerated) in 27 meta-analyses and smaller in six than the effects derived from the referent group of concealed trials. The effect of unclear allocation concealment varied among the 33 sets of trials by more than would be expected by chance ($P=.01$).

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Chisq(32df) ~ 53.5
=> Scale Parameter ~ 1.7

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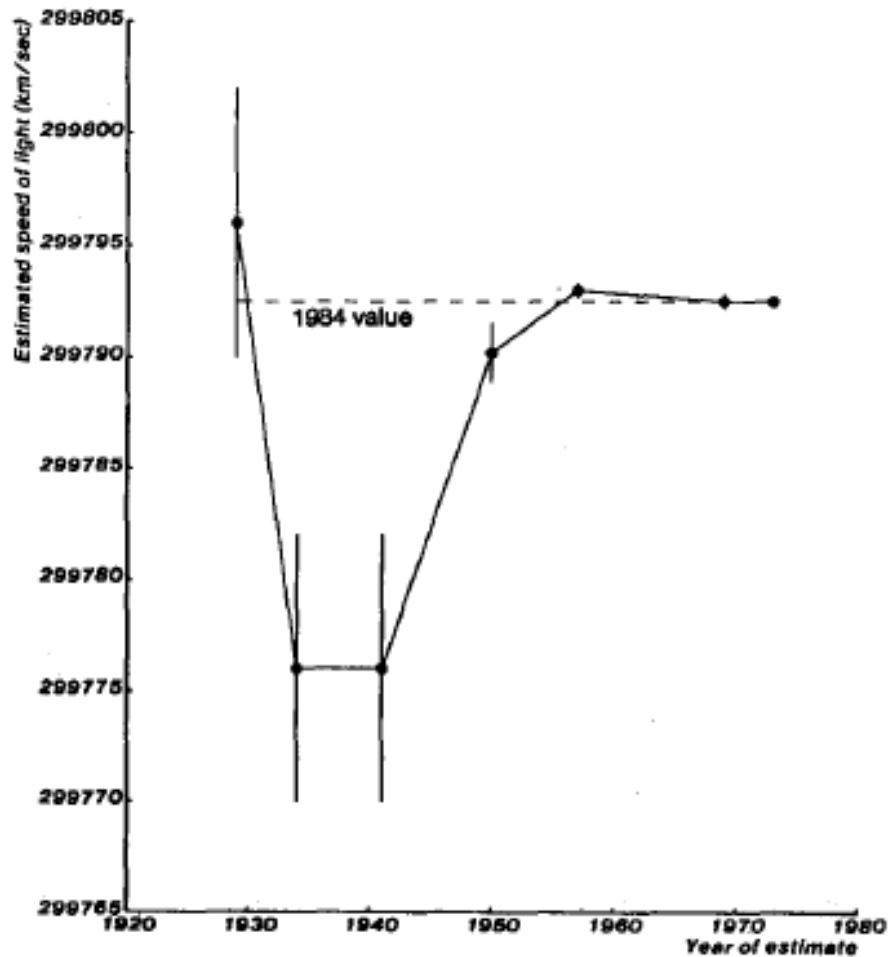We also found that estimates of treatment effects were larger in trials that had not reported double-blinding.

Fig. 2. Recommended values for the velocity of light; 1929–1973.