Small-sample adjustments for multiple-contrast hypothesis tests of meta-regressions using robust variance estimation

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Robust variance estimation (RVE)

- Robust variance estimation (RVE) is a method for constructing **asymptotically valid** SEs, hypothesis tests, and CIs when the variance or dependence structure of a regression model is **unknown** or **mis-specified**.

- In meta-analysis/meta-regression, RVE is useful for:
  - Univariate meta-analysis (Sidik & Jonkman, 2006), if sampling variances are inaccurate.
  - Meta-regression with dependent effect sizes (Hedges, Tipton, & Johnson, 2010), if correlations between effect size estimates are not available.

RVE in large samples

- RVE standard errors are **asymptotically valid,** i.e., when the number of independent studies (*m*) is sufficiently large.
  - But standard errors tend to be **too small** when *m* is small.

- For testing single meta-regression coefficients, the z-statistic (estimate / robust SE) is normally distributed if *m* is sufficiently large.
  - But z-test has **inflated Type I error** when *m* is small.

- For testing hypotheses involving multiple coefficients, a Wald statistic will follow a chi-squared distribution if *m* is sufficiently large.
  - But Wald test has **severely inflated Type-I error** if *m* is not "large enough."

Example: Wilson, Lipsey, Tanner-Smith, Huang, & Steinka-Fry (2011)

- Meta-analysis of dropout prevention/intervention programs
  - Primary outcomes: school completion, school dropout
  - m = 152 studies
  - N = 385 effect size estimates
  - Many studies provided effect size estimates for multiple outcome measures based on the same sample of participants.
- Original analysis used RVE (without small-sample correction)
- Meta-regression model including five categorical moderators.
  - E.g., Study design: randomized experiment, matched, uncontrolled

Small-sample adjustments

- Tipton (In Press) devised a small-sample correction for single-coefficient tests, involving
  - Adjustments to the RVE formula
  - Estimated degrees-of-freedom based on a Satterthwaite approximation
- Our work provides small-sample corrections for multiple-contrast hypothesis tests.
  - Tests of equality of several levels of a moderator variable
  - Tests of overall model fit

Small-sample F-test

- Linear hypothesis with q contrasts: $\mathbf{C}\boldsymbol{\beta} = \mathbf{c}$.
- We consider adjustments to the Wald statistic

$$Q = \left(\mathbf{Cb} - \mathbf{c}\right)^T \left[\mathbf{C}\mathbf{V}^R\mathbf{C}^T\right]^{-1}\left(\mathbf{Cb} - \mathbf{c}\right)$$

  where **b** is the vector of coefficient estimates and $\mathbf{V}^R$ is the robust variance estimator.

- A two-part adjustment:
  1. Following Tipton (In Press), adjust $\mathbf{V}^R$ using the McCaffrey, Bell, & Botts (2001) "bias reduced linearization" approach.
  2. Approximate the distribution of Q using an F-distribution with estimated degrees-of-freedom.
- We investigated a wide variety of different degrees-of-freedom approximations.

The Winner: AHZ

- Match mean and **total variance** of $\mathbf{CV}^R\mathbf{C}^T$ to a Wishart distribution with η degrees of freedom.

- Approximate the distribution of Q by Hotelling's T^2 distribution:

$$\left(\frac{\eta - q + 1}{\eta q}\right) \times Q \mathrel{\dot\sim} \mathrm{F}\left(\mathrm{q}, \eta - q + 1\right)$$

- In an extensive set of simulations, we found that AHZ:
  - Nearly always had Type I error less than or equal to the nominal α
  - More accurate than the other level-α corrections
  - Tended to be conservative (Type I error < α) in small samples.

Example: Wilson et al. (2011)

		χ^2 test		AHZ test		
Moderator	q	Q	p-val	F	d.f.	p-val
Study design (3 levels)	2	0.46	.796	0.22	43	.801
Outcome measure (4 levels)	3	2.74	.436	0.84	22	.489
Evaluator independence (4 levels)	3	9.33	.029	2.78	17	.073
Implementation quality (3 levels)	2	28.31	<.001	13.78	37	<.001
Program format (4 levels)	3	11.54	.011	3.65	38	.021

- Based on m = 152 studies, N = 385 effect sizes.
- Weights based on "hierarchical" model proposed by Hedges et al. (2010).

Conclusions and future work

- Small-sample corrections **should always be used** in practice.
  - The performance of the large-sample test depends on **features of the covariates** (e.g., balance, leverage), not just sample size.
  - Consequently, it is hard to say what constitutes a "large enough" sample.
- Single- and multiple-contrast hypothesis tests implemented in R package **clubSandwich**
  - Works with **metafor** (Viechtbauer, 2010) and **robumeta** (Fisher & Tipton, 2015)
  - Currently available on Github (https://github.com/jepusto/clubSandwich)
- Interested in helping us implement in Stata?

Questions?

- Working paper available upon request
- Ask about our simulation results!

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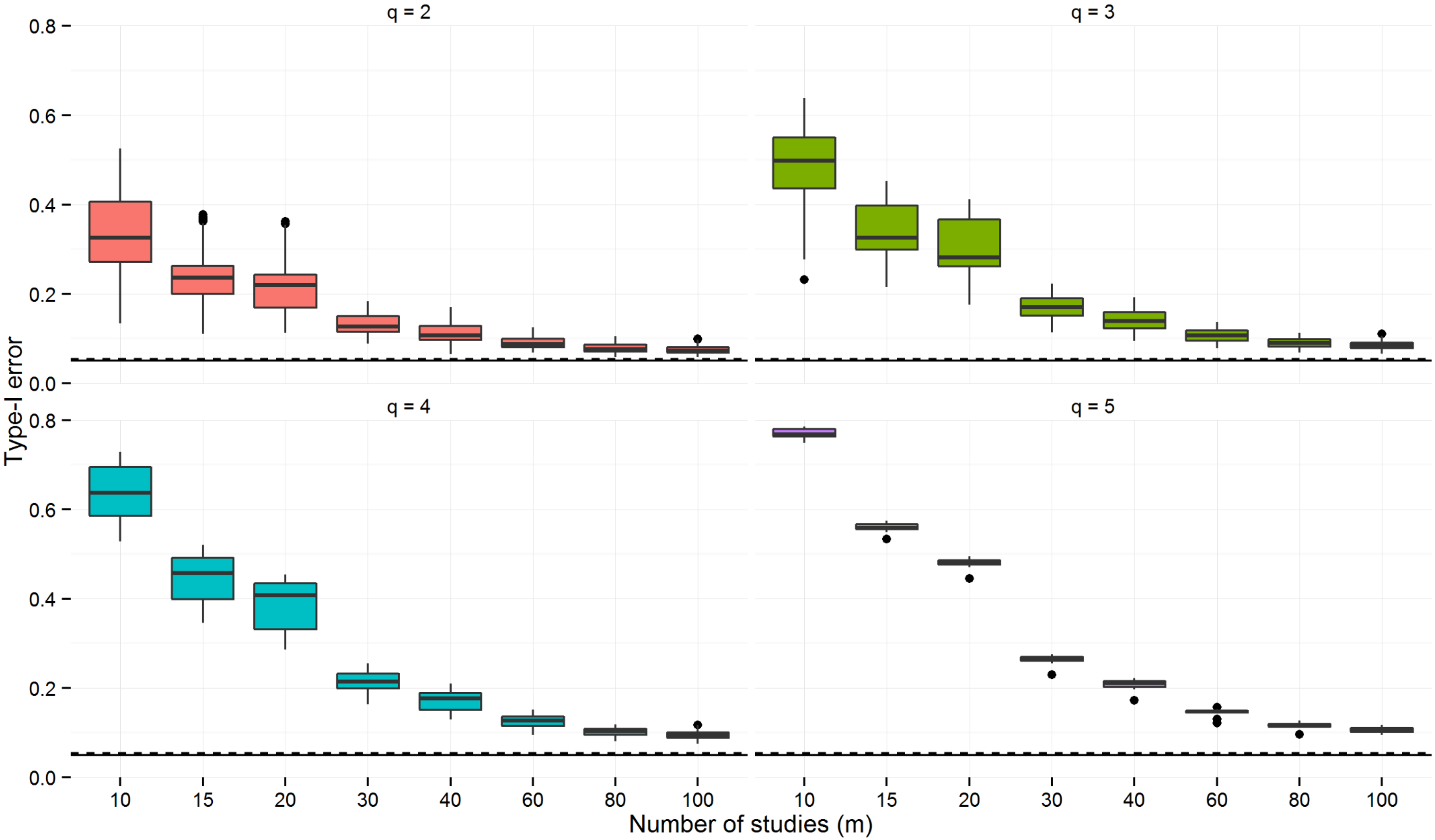
Simulated Type-I error

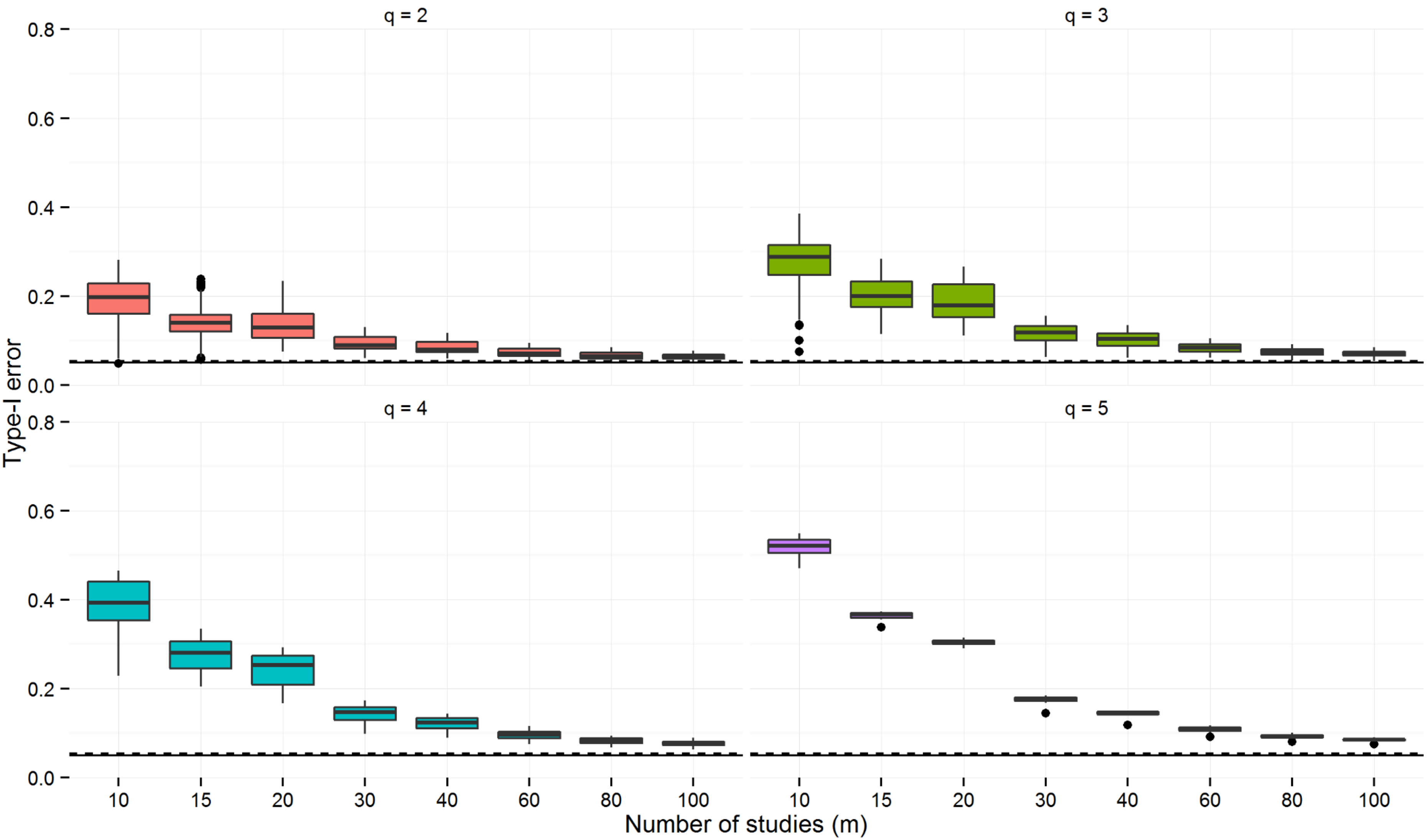
Moderator	q	χ^2 test		AHZ test	
		m = 32	*m* = 152	*m* = 32	*m* = 152
Study design (3 levels)	2	.278	.145	.073	.075
Outcome measure (4 levels)	3	.261	.155	.023	.046
Evaluator independence (4 levels)	3	.396	.175	.012	.051
Implementation quality (3 levels)	2	.248	.142	.048	.065
Program format (4 levels)	3	.383	.179	.044	.074

- Simulations based on design matrix of Wilson et al. (2011).
- *m* = 32 is the subset of 32 studies that report 3 or more effect sizes.
- Weights based on “hierarchical” model proposed by Hedges et al. (2010).
- 5000 replications.

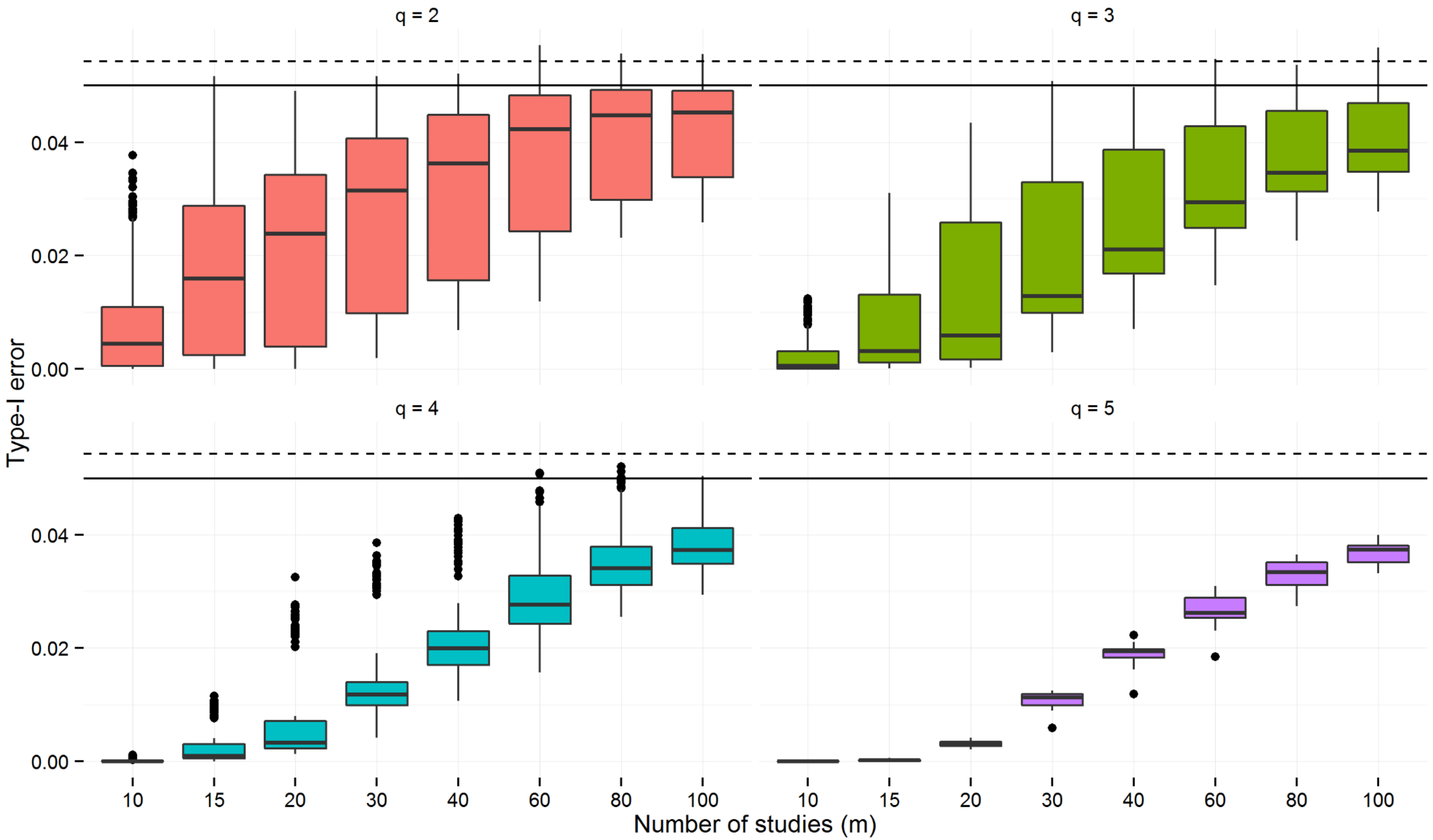
Simulated Type-I error of χ^2 test



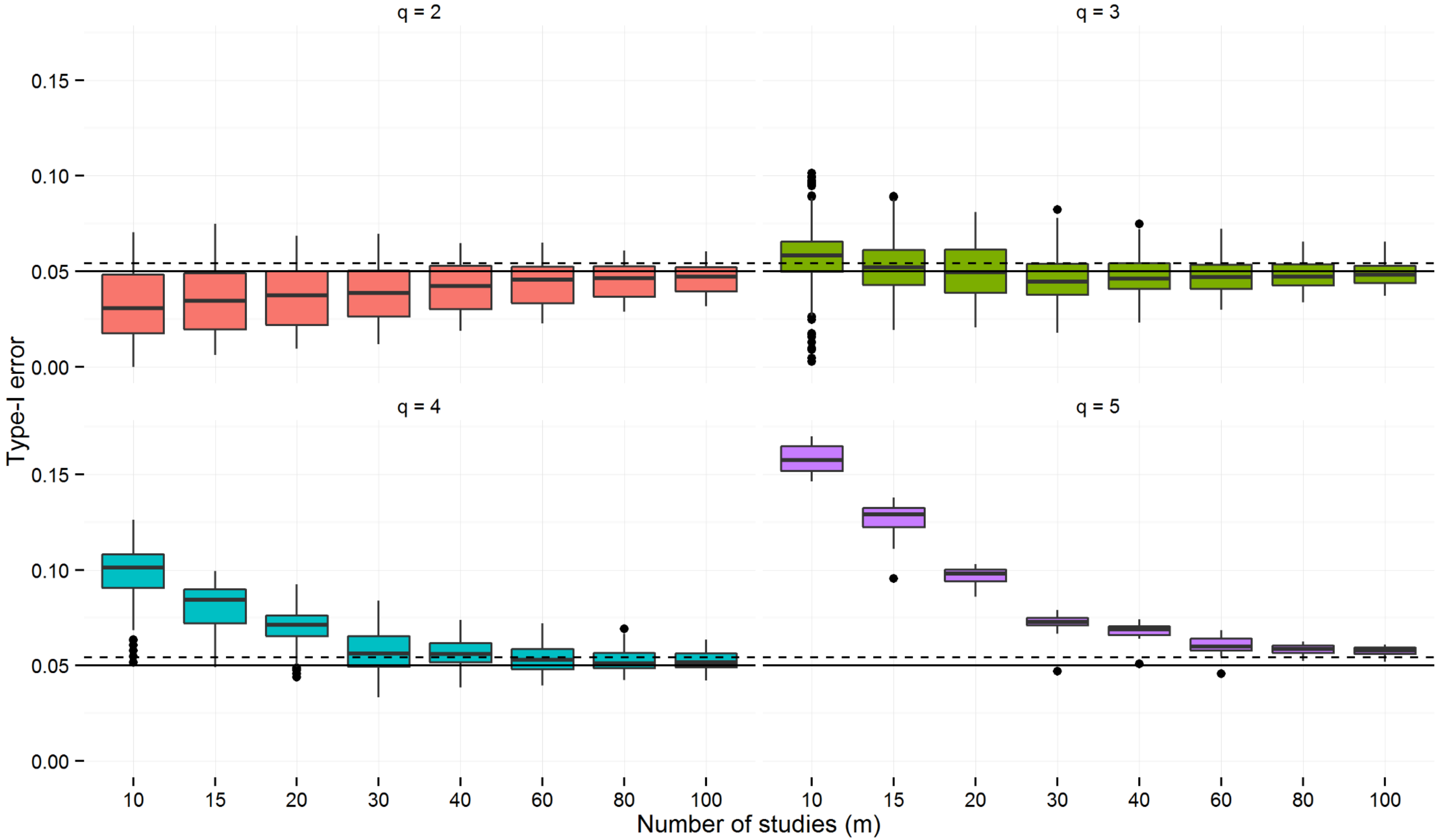
Simulated Type-I error of χ^2 test with bias-reduced linearization adjustment



Simulated Type-I error of AHZ test



Simulated Type-I error of EDT test



Bias-reduced linearization estimator

- McCaffrey, Bell, & Botts (2001) proposed a correction to $\mathbf{V}^R$ based on a working model for the error covariance structure.

- Suppose that weights are chosen to be inverse-variance under the working model. Then

$$\text{Var}(\mathbf{b}) = \left(\sum_{j=1}^{m} \mathbf{X}_j^T \mathbf{W}_j \mathbf{X}_j\right)^{-1} = \mathbf{M}.$$

- The corrected RVE is

$$\mathbf{V}^R = \mathbf{M}\left(\sum_{j=1}^{m} \mathbf{X}_j^T \mathbf{W}_j \mathbf{A}_j \mathbf{e}_j \mathbf{e}_j^T \mathbf{A}_j^T \mathbf{W}_j \mathbf{X}_j\right)\mathbf{M}$$

where the adjustment matrices $\mathbf{A}_1,\ldots,\mathbf{A}_m$ are chosen so that $E(\mathbf{V}^R) = \mathbf{M}$ when the working model is correct.