Supplementary Material to
The Direct Integral Method for Confidence Intervals for the Ratio of Two Location Parameters

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S.1 Fieller's Method

Consider a ratio $r = \mu_1/\mu_2$, where μ_1 and μ_2 are means from two correlated normal distributions $T_1 \sim \text{Normal}(\mu_1, v_1^2)$ and $T_2 \sim \text{Normal}(\mu_2, v_2^2)$. Let ρ denote the correlation coefficient between these two distributions. The estimated variance and covariance $\widehat{v}_1^2$, $\widehat{v}_2^2$ and $\widehat{\rho}\widehat{v}_1\widehat{v}_2$ are jointly estimated with the same number of degrees of freedom d, and are independent of T_1 and T_2.

Introduce a latent variable $W = T_1 - rT_2$. Since $W/\sqrt{\widehat{v}_2^2 - 2r\widehat{\rho}\widehat{v}_1\widehat{v}_2 + r^2\widehat{v}_2^2}$ follows a t distribution with d degrees of freedom, a confidence interval with coverage probability $1-\alpha$ is calculated by using $-t_{d,\alpha/2} \le W/\sqrt{\widehat{v}_2^2 - 2r\widehat{\rho}\widehat{v}_1\widehat{v}_2 + r^2\widehat{v}_2^2} \le t_{d,\alpha/2}$, where $t_{d,\alpha/2}$ denotes the $(1-\alpha/2)100\%$ quantile for the t distribution with d degrees freedom.

Rewrite the inequality and solve it as

$$r^2\{T_2^2 - t_{d,\alpha/2}^2\widehat{v}_2^2\} - 2r(T_1T_2 - t_{d,\alpha/2}^2\widehat{\rho}\widehat{v}_1\widehat{v}_2) + \{T_1^2 - t_{d,\alpha/2}^2\widehat{v}_1^2\} \le 0.$$

Let $a = T_2^2 - t_{d,\alpha/2}^2\widehat{v}_2^2, b = -2r(T_1T_2 - t_{d,\alpha/2}^2\widehat{\rho}\widehat{v}_1\widehat{v}_2)$ and $c = T_1^2 - t_{d,\alpha/2}^2\widehat{v}_1^2$. Following the inequality $ar^2 + br + c \le 0$, two real roots $(-b \pm \sqrt{b^2 - 4ac})/(2a)$ are obtained if $b^2 - 4ac \ge 0$.

Define d_1 as the smaller value of roots and d_2 as the larger one, and then a confidence interval of r which has coverage probability $1-\alpha$ is constructed as follows:

$$\text{Confidence Interval} = \begin{cases} (d_1, d_2) & \text{if } a \ge 0, \\ (-\infty, d_1)\bigcup(d_2, \infty) & \text{if } a < 0 \text{ and } t_{d,\alpha/2} < t_{com}, \\ (-\infty, \infty) & \text{if } t_{d,\alpha/2} \ge t_{com}, \end{cases}$$

where $t_{com} = (T_1^2\widehat{v}_2^2 - 2T_1T_2\widehat{v}_{12} + T_2^2\widehat{v}_1^2)/(\widehat{v}_1^2\widehat{v}_2^2 - \widehat{v}_{12}^2)$ and it is certain that $a < 0$ when $t_{d,\alpha/2} > t_{com}$ as Fieller (1954) showed that $T_2^2/\widehat{v}_2^2 \le t_{com}^2$.

There are several limitations of Fieller's algorithm. First, $b^2 - 4ac \geq 0$ is required; otherwise the inequality function has two complex roots. Second, when a decreases to 0, the interval range increases rapidly and can become infinite. Finally, if a is negative, the confidence interval is deterministic to have infinite length.

S.2 Proofs of the Technical Results

Proof of Lemma 1:

Lemma 1 follows because

$$\begin{aligned}
\mathrm{pr}(\widehat{r} \leq x) &= \mathrm{pr}(T_1 \leq xT_2, T_2 > 0) + \mathrm{pr}(T_1 \geq xT_2, T_2 < 0) \\
&= \int_0^\infty \int_{-\infty}^{xt_2} (v_1 v_2)^{-1} f_1\{(t_1 - \mu_1)/v_1\} f_2\{(t_2 - \mu_2)/v_2\} dt_1 dt_2 \\
&\quad + \int_{-\infty}^0 \int_{xt_2}^\infty (v_1 v_2)^{-1} f_1\{(t_1 - \mu_1)/v_1\} f_2\{(t_2 - \mu_2)/v_2\} dt_1 dt_2 \\
&= \int_0^\infty F_1\{(xt_2 - \mu_1)/v_1\} v_2^{-1} f_2\{(t_2 - \mu_2)/v_2\} dt_2 \\
&\quad + \int_{-\infty}^0 [1 - F_1\{(xt_2 - \mu_1)/v_1\}] v_2^{-1} f_2\{(t_2 - \mu_2)/v_2\} dt_2 \\
&\overset{z=(t_2-\mu_2)/v_2}{=} \int_{-\mu_2/v_2}^\infty F_1[\{x(\mu_2 + v_2 z) - \mu_1\}/v_1] f_2(z) dz \\
&\quad + \int_{-\infty}^{-\mu_2/v_2} (1 - F_1[\{x(\mu_2 + v_2 z) - \mu_1\}/v_1]) f_2(z) dz.
\end{aligned}$$

For simplicity, define $g(z|x, \mu_1, \mu_2, v_1, v_2)$ as in Section 2.2. Then we have the cumulative distribution function of $\widehat{r} = T_1/T_2$ as

$$\mathrm{pr}(\widehat{r} \leq x) = \int_{-\infty}^\infty g(z|x, \mu_1, \mu_2, v_1, v_2) \exp(-z^2) dz.$$

Proof of Lemma 2:

In the normal T_1 and T_2 case, $F_1(z)$ and $f_2(z)$ in Lemma 1 are the standard normal cumulative distribution and density functions, respectively. Since $\widehat{v}_1^2 = v_1^2 + O_p(d_1^{-1/2}) = O_p(d^{-1/2})$ and $\widehat{v}_2^2 = v_2^2 + O_p(d_2^{-1/2}) = O_p(d^{-1/2})$, we have that $g(z|x, \mu_1, \mu_2, v_1, v_2) = g(z|x, \mu_1, \mu_2, \widehat{v}_1, \widehat{v}_2) + O_p(d^{-1/2})$.

On the other hand, by a Taylor series expansion of the t_{d_2} density function, $f_{t,d_2}(z)$, reveals that $f_{t,d_2}(z) = f_2(z) + O(d_2^{-1})$. The same result for the t_{d_1} density function leads to the following expansion for its cumulative distribution function: $F_{t,d_1}[\{x(\mu_2 + \widehat{v}_2 z) - \mu_1\}/v_1] =$

$F_1[\{x(\mu_2+v_2z)-\mu_1\}/v_1]+O(d_1^{-1})$. Combining the two approximations above, we obtain that

$$g(z|x,\mu_1,\mu_2,\widehat{v}_1,\widehat{v}_2)=h(z|x,\mu_1,\mu_2,\widehat{v}_1,\widehat{v}_2)+O_p(d^{-1}).$$

Thus, by Lemma 1,

$$\begin{aligned}\mathrm{pr}(\widehat{r}\le x) &= \int_{-\infty}^{\infty} g(z|x,\mu_1,\mu_2,v_1,v_2)\exp(-z^2)dz\\ &= \int_{-\infty}^{\infty} g(z|x,\mu_1,\mu_2,\widehat{v}_1,\widehat{v}_2)\exp(-z^2)dz+O_p(d^{-1/2})\\ &= \int_{-\infty}^{\infty} g(z|x,\mu_1,\mu_2,\widehat{v}_1,\widehat{v}_2)\exp(-z^2)dz+O_p(d^{-1/2}).\end{aligned}$$

<u>Proof of Lemma 3:</u>

Letting $V=\mathrm{cov}(T_1,T_2)$ Lemma 3 follows from the fact that

$$\begin{aligned}&\mathrm{pr}(\widehat{r}\le x)\\ &= \int_0^{\infty}\int_{-\infty}^{xt_2}(2\pi|v_1^2v_2^2-v_{12}^2|^{1/2})^{-1}\exp\{-(t_1-\mu_1,t_2-\mu_2)V^{-1}(t_1-\mu_1,t_2-\mu_2)^{\mathrm{T}}/2\}dt_1dt_2\\ &+\int_{-\infty}^{0}\int_{xt_2}^{\infty}(2\pi|v_1^2v_2^2-v_{12}^2|^{1/2})^{-1}\exp\{-(t_1-\mu_1,t_2-\mu_2)V^{-1}(t_1-\mu_1,t_2-\mu_2)^{\mathrm{T}}/2\}dt_1dt_2\\ &\overset{z=(t_2-\mu_2)/v_2}{=} (2\pi)^{-1/2}\int_{-\mu_2/v_2}^{\infty}\Phi[\{x(\mu_2+v_2z)-(\mu_1+zv_{12}/v_2)\}v_2/\sqrt{v_1^2v_2^2-v_{12}^2}]\exp(-z^2/2)dz\\ &+(2\pi)^{-1/2}\int_{-\infty}^{-\mu_2/v_2}(1-\Phi[\{x(\mu_2+v_2z)-(\mu_1+zv_{12}/v_2)\}v_2/\sqrt{v_1^2v_2^2-v_{12}^2}])\exp(-z^2/2)dz.\end{aligned}$$

Define $g(z|x,\mu_1,\mu_2,v_1^2,v_2^2,v_{12})$ as in Section 2.3. Then the cumulative distribution function of $\widehat{r}$ is

$$\mathrm{pr}(\widehat{r}\le x)=\int_{-\infty}^{\infty} g(z|x,\mu_1,\mu_2,v_1^2,v_2^2,v_{12})\exp(-z^2)dz,$$

<u>Proof of Equation (1) in Section 2.4:</u>

Define $Z_1=\{(T_1-rT_2)-(\mu_1-r\mu_2)\}/\sqrt{\widehat{v}_1^2-2\eta\widehat{v}_{12}+\eta^2\widehat{v}_2^2}$ and $Z_2=(T_2-\mu_2)/\widehat{v}_2$ in Section 2.4, respectively. Then Z_1 and Z_2 are independent and both have t distributions with degree freedom of d. Therefore, the jointly density distribution of Z_1 and Z_2 is

$$f(Z_1,Z_2)=f_{t,d}(Z_1)f_{t,d}(Z_2),$$

where $f_{t,d}$ is the standard student t density with degree of freedom d. Using the fact that $\widehat{v}_i=v_i+O_p(d^{-1/2})$ for $i=1,2,12$ and the density transform method the jointly distribution of (T_1, T_2) can be approximated as follows:

$$f(T_1, T_2) = \widehat{v}_2^{-1}(\widehat{v}_1^2 - 2\eta\widehat{v}_{12} + \eta^2\widehat{v}_2^2)^{-1/2}$$
$$f_{t,d}[\{(t_1 - dt_2) - (\mu_1 - \eta\mu_2)\}/\sqrt{\widehat{v}_1^2 - 2\eta\widehat{v}_{12} + \eta^2\widehat{v}_2^2}]f_{t,d}\{(t_2 - \mu_2)/\widehat{v}_2\} + O_p(d^{-1/2}).$$

Letting $z = (t_2 - \mu_2)/\widehat{v}_2$, and defining $g(z|x, \mu_1, \mu_2, \widehat{v}_1^2, \widehat{v}_2^2, \widehat{v}_{12}, \eta)$ as in Section 2.4, we get the cumulative distribution function of $\widehat{r} = T_1/T_2$ as

$$\text{pr}(\widehat{r} \leq x) = \int_{-\infty}^{\infty} g(z|x, \mu_1, \mu_2, \widehat{v}_1^2, \widehat{v}_2^2, \widehat{v}_{12}, \eta)\exp(-z^2)dz + O_p(d^{-1/2}).$$

S.3 Hayya's Method

The method was proposed by Hayya et al. (1975) in a not very well-known article. They suggested a normal approximation to the true cumulative distribution function of the ratio $\widehat{r} = T_1/T_2$ obtained by a second order Taylor expansion. By Monte Carlo simulations, they concluded that if the absolute value of the correlation between T_1 and T_2 is less or equal to 0.5, the coefficient of variation of T_2 is less or equal to 0.09 and the coefficient of variation of T_1 is larger than 0.19, the ratio $\widehat{r} = T_1/T_2$ is approximately normally distributed with

$$\begin{aligned} E(\widehat{r}) &\approx (\mu_1/\mu_2) + v_2^2\mu_1/\mu_2^3 - \rho v_2 v_1/\mu_2^2, \\ \text{var}(\widehat{r}) &\approx v_2^2\mu_1^2/\mu_2^4 + v_1^2/\mu_2^2 - 2\rho v_2 v_1 \mu_1/\mu_2^3, \end{aligned}$$

where ρ is the correlation between T_1 and T_2 and $\widehat{r}$ is corresponding to $\widehat{\beta}_{21}$ in the model (2).

S.4 Starting Values for the Algorithm in Section 2.5

We start two points $d_{10} < 0$ and $d_{20} > 0$.

For d_{10},

1. Set $d_{10} = -100$.
2. Compute $F(d_{10})$. If $F(d_{10}) > \alpha/2$, let $d_{10} = d_{10} * 10$.
3. Repeat step 2 until $F(d_{10}) < \alpha/2$.

For d_{20},

1. Set $d_{20} = 100$.
2. Compute $F(d_{20})$. If $F(d_{20}) < \alpha/2$, let $d_{20} = d_{20} * 10$.
3. Repeat step 2 until $F(d_{20}) > \alpha/2$.

Then use $\widehat{r}_{\alpha_1} = d_{10}$ and $\widehat{r}_{\alpha_2} = d_{20}$. A similar procedure is used to obtain $\widehat{r}_{1-\alpha/2|\widehat{\mu}_1/\widehat{\mu}_2}$.

S.5 Some Bootstrap Details

Here are the general steps we used for the nonparametric bootstrap and parametric bootstrap.

- Procedure for the nonparametric bootstrap:
  - For given data set (Y_1, Y_2, X_1, X_2), obtain the estimates $(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega})$.
  - Generate $B = 400$ bootstrap data sets with replacement for two subgroups separately.
  - For the b^{th} generated data set $(Y_{1,b}, Y_{2,b}, X_{1,b}, X_{2,b})$, obtain $(\widehat{\beta}_{10,b}, \widehat{\beta}_{20,b}, \widehat{\beta}_{21,b}, \widehat{\omega}_b)$. Repeat this process for all resampled data sets.
  - Compute the standard error of $\widehat{\beta}_{21,b}$ as $\text{se}_{\beta_{21},\text{nonpara,boot}}$.
  - Construct the $(1-\alpha)100\%$ confidence interval: $(\widehat{\beta}_{21} - z_{\alpha/2}\text{se}_{\beta_{21},\text{nonpara,boot}}, \widehat{\beta} + z_{\alpha/2}\text{se}_{\beta_{21},\text{nonpara,boot}})$.
- Procedure for the parametric bootstrap:
  - For given data set (Y_1, Y_2, X_1, X_2), obtain the estimates $(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega})$.
  - Fix $(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega})$ and (X_1, X_2), we generate $B = 400$ data sets of $(Y_{1,b}, Y_{2,b})$ using a parametric model.
  - For the b^{th} generated data set $(Y_{1,b}, Y_{2,b})$ with (X_1, X_2), obtain $(\widehat{\beta}_{10,b}, \widehat{\beta}_{20,b}, \widehat{\beta}_{21,b}, \widehat{\omega}_b)$. Repeat this process for all resampled data sets.
  - Compute the estimated standard error of $\widehat{\beta}_{21,b}$ as $\text{se}_{\beta_{21},\text{para,boot}}$.
  - Construct the $(1-\alpha)100\%$ confidence interval: $(\widehat{\beta}_{21} - z_{\alpha/2}\text{se}_{\beta_{21},\text{para,boot}}, \widehat{\beta} + z_{\alpha/2}\text{se}_{\beta_{21},\text{para,boot}})$.

S.6 Linear Model with Two Dependent Estimates

S.6.1 Setup

We now consider another simple linear regression model:

$$Y_i = \beta(X_i + \mu) + \epsilon_i, i = 1, ..., n,$$

where the parameter of interest μ is the ratio between the intercept $\beta\mu$ and the slope β, and ϵ_i is independent and identically normally distributed with mean zero. As described in Section 3.2, this model arises in radioimmunoassay when the goal is to estimate the ID_{50}.

Let $\lambda = \beta\mu$. Then the model is rewritten as $Y_i = \lambda + \beta X_i + \epsilon_i$. Define the mle of (λ, β) as $(\widehat{\lambda}, \widehat{\beta})$. Write the estimated variances as $\widehat{v}^2_{\widehat{\lambda}}$ and $\widehat{v}^2_{\widehat{\beta}}$, and the estimated covariance as $\widehat{v}_{\widehat{\lambda},\widehat{\beta}}$, where $\widehat{v}^2_{\widehat{\lambda}}$, $\widehat{v}^2_{\widehat{\beta}}$ and $\widehat{v}_{\widehat{\lambda},\widehat{\beta}}$ are independent of $\widehat{\lambda}$ and $\widehat{\beta}$ and jointly estimated with the same degrees of freedom $n-2$.

Under these conditions, this case is particularly suitable for the application of Fieller's interval. Our intention here is to illustrate that a confidence interval constructed by our DIMER performs at least equally or even better than Fieller's interval in terms of coverage rates, but without Fieller's method's limitations on confidence interval length. Of course, we also computed the other six methods.

S.6.2 Simulation Results

We performed simulations on two test cases to compare the performance of the seven methods of forming confidence intervals: the inverse Fisher score, Hayya's method, the nonparametric bootstrap, the parametric bootstrap, Fieller's interval, DIMER, and the likelihood ratio test.

We generated X_i independently from standard normal distribution. The number of simulations was 2000 and there were 400 bootstrap replications for each simulation. We set $(\beta, \mu) = (-1.00, 1.00)$. We simulated both the normal case where $\epsilon = \mathrm{Normal}(0, 1)$, see Table S.1, and the case that ϵ_i follows a skew-normal distribution with mean 0, variance 1 and skewness 0.78, see Table S.2. In such a circumstance, neither $\widehat{\beta}\widehat{\mu}$ nor $\widehat{\mu}$ is normally distributed. Both cases were evaluated with sample sizes of $10, 25, 50$. Since the methods were all comparable when $n = 50$, we focus on $n = 10$ and $n = 25$.

Tables 1-2 suggested that DIMER achieved its nominal coverage probability lengths without the infinite length intervals of Fieller's method, and without the less than nominal coverage probabilities of the inverse Fisher score and Hayya's method.

In Tables S.1-S.2, we see that DIMER achieves its nominal coverage in all cases. The inverse Fisher score method had better coverage than in Tables 1-2, yet still had distinctly sub-nominal coverage for $n = 10$, as did Hayya's method and the likelihood ratio test. In addition, when $n = 10$ there were rather large probabilities for the likelihood ratio test and Fieller's method to generate infinite length. The parametric bootstrap was somewhat sub-nominal in Tables S.1-S.2, while the nonparametric bootstrap was close to nominal except for the 99% confidence intervals. Especially for $n = 10$, Fieller's interval often resulted in infinite confidence intervals, although it achieved its nominal coverage probabilities. Of course, by always achieving the nominal levels, DIMER and Fieller's method cannot be expected to have shorter confidence interval lengths, especially with $n = 10$, but by $n = 25$ the former had roughly comparable lengths.

The results of Tables 1-2 and Tables S.1-S.2 suggest that because it achieves its nominal coverage probability, DIMER has advantages compared to the other methods, although it does not always dominate the others in those cases that the others manage to achieve nominal coverage probability.

Method	Mean of Coverage 90% CI	95% CI	99% CI	Mean of Length 90% CI	95% CI	99% CI	Median of Length 90% CI	95% CI	99% CI	90% Quantile of Length 90% CI	95% CI	99% CI
$n = 10, \mathrm{cv}(\widehat{\beta}) = -0.38, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.34, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.01, 1.26), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-0.99, 0.99)$												
IF	87.50	90.90	94.95	11.94	14.22	18.69	1.45	1.73	2.28	4.46	5.31	6.98
HM	83.45	89.05	94.25	11.94	14.22	18.69	1.45	1.73	2.28	4.46	5.31	6.98
NB	93.50	95.05	96.55	67.68	80.65	106.0	6.61	7.88	10.36	108.9	129.8	170.6
PB	91.50	93.35	96.30	101.0	120.3	158.1	3.86	4.60	6.05	125.7	149.8	196.8
FI	92.40	96.65	99.20	∞	∞	∞	2.41	3.86	∞	∞	∞	∞
DIMER	93.10	96.85	99.05	7.20	22.94	96.91	2.24	3.41	13.54	12.29	30.73	125.7
LR Test	84.95	91.65	97.70	∞	∞	∞	1.81	2.69	14.21	∞	∞	∞
INL–LR	14.8%	23.8%	49.6%									
INL–FI	18.9%	30.4%	59.8%									
$n = 25, \mathrm{cv}(\widehat{\beta}) = -0.21, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.20, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.01, 1.04), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.01, 1.00)$												
IF	89.75	93.10	96.90	1.07	1.27	1.67	0.93	1.11	1.46	1.64	1.95	2.57
HM	89.15	93.55	97.00	1.07	1.27	1.67	0.93	1.11	1.46	1.64	1.95	2.57
NB	91.10	93.95	97.45	15.02	17.90	23.52	1.09	1.29	1.70	6.39	7.62	10.01
PB	91.70	94.70	97.75	4.88	5.82	7.65	1.08	1.29	1.69	3.62	4.32	5.68
FI	89.45	95.10	98.75	∞	∞	∞	1.07	1.36	2.15	2.21	3.12	9.03
DIMER	89.70	95.10	98.70	1.36	2.16	6.26	1.07	1.36	2.12	2.18	3.02	6.67
LR Test	87.45	93.35	98.25	∞	∞	∞	1.00	1.26	1.95	2.02	2.77	6.40
INL–LR	0.2%	1.0%	5.5%									
INL–FI	0.2%	0.9%	4.5%									
$n = 50, \mathrm{cv}(\widehat{\beta}) = -0.14, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.00, 1.02), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.01, 1.00)$												
IF	91.40	95.80	98.50	0.70	0.83	1.10	0.65	0.78	1.02	0.96	1.15	1.51
HM	91.05	95.60	98.60	0.70	0.83	1.10	0.65	0.78	1.02	0.96	1.15	1.51
NB	91.90	95.95	98.40	0.86	1.03	1.35	0.69	0.82	1.08	1.15	1.37	1.79
PB	93.15	96.50	98.80	0.80	0.96	1.26	0.69	0.82	1.08	1.11	1.32	1.74
FI	91.60	95.75	99.40	0.76	0.94	∞	0.70	0.85	1.20	1.07	1.34	2.02
DIMER	91.65	95.75	99.40	0.76	0.94	1.38	0.70	0.85	1.19	1.07	1.34	2.01
LR Test	90.25	95.35	99.35	0.74	0.91	∞	0.68	0.83	1.16	1.04	1.30	1.93
INL–LR	0.0%	0.0%	0.1%									
INL–FI	0.0%	0.0%	0.1%									

Table S.1: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i+\mu)+\epsilon_i$ with $(\beta, \mu) = (-1.00, 1.00)$, where ϵ_i follows a normal distribution with mean 0, variance 1. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \mathrm{cv}(\widehat{\beta}) = -0.38, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.35, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-0.99, 1.25), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.00, 1.03)$												
IF	86.75	91.05	95.65	11.45	13.65	17.93	1.47	1.75	2.30	4.81	5.73	7.53
HM	80.65	87.60	93.60	11.45	13.65	17.93	1.47	1.75	2.30	4.81	5.73	7.53
NB	92.90	94.50	96.75	93.80	111.8	146.9	5.80	6.91	9.08	112.4	133.9	176.0
PB	90.55	93.35	96.05	153.0	182.3	239.6	3.79	4.51	5.93	139.6	166.4	218.7
FI	90.15	95.05	98.75	∞	∞	∞	2.31	3.58	∞	∞	∞	∞
DIMER	90.90	95.55	98.75	8.45	16.23	69.22	2.26	3.35	12.68	13.25	35.06	110.5
LR Test	83.10	89.65	97.20	∞	∞	∞	1.82	2.64	11.63	∞	∞	∞
INL–LR	16.8%	24.6%	48.7%									
INL–FI	21.0%	30.5%	57.1%									
$n = 25, \mathrm{cv}(\widehat{\beta}) = -0.22, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.21, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-0.99, 1.05), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-0.99, 1.02)$												
IF	89.00	93.20	97.70	1.09	1.30	1.71	0.93	1.11	1.45	1.66	1.98	2.60
HM	88.15	93.65	97.65	1.09	1.30	1.71	0.93	1.11	1.45	1.66	1.98	2.60
NB	91.65	94.95	98.20	13.29	15.84	20.81	1.09	1.30	1.71	7.84	9.35	12.28
PB	92.10	95.30	98.25	15.18	18.09	23.77	1.08	1.29	1.69	4.58	5.45	7.17
FI	89.35	94.55	98.50	∞	∞	∞	1.06	1.36	2.18	2.28	3.33	10.40
DIMER	89.90	94.60	98.45	1.51	2.98	10.80	1.07	1.35	2.14	2.24	3.18	7.58
LR Test	87.45	93.05	97.85	∞	∞	∞	1.00	1.25	1.96	2.10	2.93	7.44
INL–LR	0.7%	1.7%	6.9%									
INL–FI	0.7%	1.6%	6.2%									
$n = 50, \mathrm{cv}(\widehat{\beta}) = -0.14, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.00, 1.02), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.00, 1.01)$												
IF	90.80	95.25	98.60	0.69	0.82	1.08	0.65	0.78	1.02	0.95	1.13	1.48
HM	90.50	95.30	98.60	0.69	0.82	1.08	0.65	0.78	1.02	0.95	1.13	1.48
NB	91.50	95.60	99.00	0.83	0.99	1.30	0.68	0.81	1.06	1.04	1.24	1.63
PB	92.65	96.15	99.05	0.76	0.91	1.20	0.69	0.82	1.08	1.08	1.28	1.69
FI	90.70	95.50	98.85	0.75	0.92	1.34	0.69	0.85	1.20	1.05	1.30	1.94
DIMER	90.70	95.40	98.85	0.75	0.92	1.33	0.70	0.85	1.19	1.05	1.30	1.93
LR Test	90.00	94.90	98.75	0.73	0.89	1.29	0.68	0.82	1.16	1.02	1.26	1.87
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.2: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (-1.00, 1.00)$, where ϵ_i follows a skewed normal distribution with mean 0, variance 1 and skewness 0.78. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

Component	Units	HEI-2005 score calculation
Total Fruit	cups	$\min(5, 5 \times (\text{density}/.8))$
Whole Fruit	cups	$\min(5, 5 \times (\text{density}/.4))$
Total Grains	ounces	$\min(5, 5 \times (\text{density}/3))$
Whole Grains	ounces	$\min(5, 5 \times (\text{density}/1.5))$
Total Vegetables	cups	$\min(5, 5 \times (\text{density}/1.1))$
DOL	cups	$\min(5, 5 \times (\text{density}/.4))$
Milk	cups	$\min(10, 10 \times (\text{density}/1.3))$
Meat and Beans	ounces	$\min(10, 10 \times (\text{density}/2.5))$
Oil	grams	$\min(10, 10 \times (\text{density}/12))$
Saturated Fat	% of energy	if density $\geq$ 15 score = 0 else if density $\leq$ 7 score = 10 else if density $>$ 10 score $= 8 - (8 \times (\text{density} - 10)/5)$ else, score $= 10 - (2 \times (\text{density} - 7)/3)$
Sodium	milligrams	if density $\geq$ 2000 score=0 else if density $\leq$ 700 score=10 else if density $\geq$ 1100 score $= 8 - \{8 \times (\text{density} - 1100)/(2000 - 1100)\}$ else score $= 10 - \{2 \times (\text{density} - 700)/(1100 - 700)\}$
SoFAAS	% of energy	if density $\geq$ 50 score = 0 else if density $\leq$ 20 score=20 else score $= 20 - \{20 \times (\text{density} - 20)/(50 - 20)\}$

Table S.3: Description of the HEI-2005 scoring system. Except for saturated fat and SoFAAS, density is obtained by multiplying usual intake by 1000 and dividing by usual intake of kilo-calories. For saturated fat, density is 9×100 usual saturated fat (grams) divided by usual calories, i.e., the percentage of usual calories coming from usual saturated fat intake. For SoFAAS, the density is the percentage of usual intake that comes from usual intake of calories, i.e., the division of usual intake of SoFAAS by usual intake of calories. Here, "DOL" is dark green and orange vegetables and legumes. Also, "SoFAAS" is calories from solid fats, alcoholic beverages and added sugars. The total HEI-2005 score is the sum of the individual component scores.

S.7 Additional Simulations

Here we list the results of numerous other simulations.

- Table S.4 considers model (2) in Section 3.4.1 when $(n, v_\epsilon) = (55, 2.0)$ and $(115, 3.0)$. The purpose of this table is to illustrate what happens with larger sample sizes and more noise in the regression model.
- Table S.5 considers the model in Section S.6.1 with $(\beta, \mu) = (1.00, 1.00)$.
- Table S.6 considers the model in Section S.6.1 with $(\beta, \mu) = (1.00, -1.00)$.
- Table S.7 considers the model in Section S.6.1 with $(\beta, \mu) = (-1.00, -1.00)$.
- Table S.8 considers the model in Section S.6.1 with the skew-normal regression errors and $(\beta, \mu) = (1.00, 1.00)$.
- Table S.9 considers the model in Section S.6.1 with the skew-normal regression errors and $(\beta, \mu) = (1.00, -1.00)$.
- Table S.10 considers the model in Section S.6.1 with the skew-normal regression errors and $(\beta, \mu) = (-1.00, -1.00)$.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n_1 = n_2 = 55, v_{\epsilon_1} = v_{\epsilon_2} = 2, \mathrm{cv}(\widehat{\omega}) = 0.27, \mathrm{cv}(\widehat{\lambda}) = 0.29$												
$\mathrm{mean}(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega}) = (0.00, 0.00, 1.09, 1.01), \mathrm{median}(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega}) = (0.01, -0.00, 1.00, 1.01)$												
IF	87.40	92.20	96.90	2.04	2.44	3.20	1.25	1.49	1.96	3.26	3.88	5.10
HM	89.60	93.90	97.45	1.70	2.02	2.66	1.27	1.51	1.99	2.60	3.10	4.07
NB	92.40	95.05	97.95	89.88	107.10	140.75	1.80	2.15	2.82	33.91	40.41	53.11
PB	93.00	94.95	97.85	36.99	44.07	57.92	1.79	2.14	2.81	33.97	40.48	53.20
FI	91.35	96.10	99.50	∞	∞	∞	1.50	1.96	3.45	5.01	10.91	∞
DIMER	91.90	96.75	99.55	4.41	9.91	41.25	1.52	1.99	3.55	4.21	7.10	62.23
LR Test	89.25	94.20	99.15	∞	∞	∞	1.46	1.91	3.37	4.75	9.95	∞
INL–LR	3.4%	6.5%	21.1%									
INL–FI	2.8%	5.1%	16.8%									
$n_1 = n_2 = 115, v_{\epsilon_1} = v_{\epsilon_2} = 3, \mathrm{cv}(\widehat{\omega}) = 0.28, \mathrm{cv}(\widehat{\lambda}) = 0.29$												
$\mathrm{mean}(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega}) = (0.01, 0.00, 1.39, 1.00), \mathrm{median}(\widehat{\beta}_{10}, \widehat{\beta}_{20}, \widehat{\beta}_{21}, \widehat{\omega}) = (0.00, 0.00, 0.98, 1.00)$												
IF	88.45	91.90	96.25	2.46	2.93	3.85	1.28	1.53	2.01	3.24	3.86	5.07
HM	89.20	93.05	96.15	197.70	235.58	309.60	1.31	1.57	2.06	2.75	3.28	4.31
NB	92.05	94.60	97.15	34.76	41.42	54.43	1.97	2.34	3.08	41.03	48.89	64.25
PB	91.95	94.30	97.15	35.44	42.22	55.49	1.97	2.35	3.09	38.62	46.02	60.48
FI	90.40	95.20	99.15	∞	∞	∞	1.58	2.09	3.80	5.15	10.92	∞
DIMER	91.20	95.60	99.20	3.38	10.35	33.21	1.59	2.10	3.82	4.44	7.20	61.10
LR Test	88.60	93.90	98.75	∞	∞	∞	1.56	2.06	3.78	5.03	10.42	∞
INL–LR	4.1%	7.1%	23.3%									
INL–FI	3.6%	5.8%	17.4%									

Table S.4: Confidence intervals for β_{21} in a simulation study with 2000 replications and true parameter values $(\beta_{10}, \beta_{20}, \beta_{21}, \omega) = (0.00, 0.00, 1.00, 1.00)$ for the linear regression model $Y_{1i} = \beta_{10} + X_{1i}\omega + \epsilon_{1i}; Y_{2j} = \beta_{20} + \beta_{21}X_{2j}\omega + \epsilon_{2j}$. Here $v_{\epsilon_i}^2 = \mathrm{var}(\epsilon_{i1})$ for $i = 1, 2$. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \text{cv}(\widehat{\beta}) = 0.39, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.34, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (0.99, 0.98), \text{median}(\widehat{\beta}, \widehat{\mu}) = (1.01, 0.99)$												
IF	88.10	91.75	95.75	75.30	89.72	117.9	1.46	1.74	2.29	4.86	5.79	7.61
HM	83.05	88.95	94.15	75.30	89.72	117.9	1.46	1.74	2.29	4.86	5.79	7.61
NB	93.00	95.05	97.00	232.2	276.7	363.7	6.40	7.62	10.02	137.6	163.9	215.4
PB	91.10	93.75	96.30	229.3	273.2	359.0	3.97	4.72	6.21	119.5	142.4	187.2
FI	92.50	96.30	99.65	∞	∞	∞	2.41	3.87	∞	∞	∞	∞
DIMER	92.95	96.50	99.55	12.21	23.18	79.26	2.27	3.42	13.63	14.29	36.57	130.7
LR Test	85.70	91.70	97.85	∞	∞	∞	1.85	2.68	12.79	∞	∞	∞
INL–LR	16.2%	24.4%	49.5%									
INL–FI	20.4%	31.0%	59.5%									
$n = 25, \text{cv}(\widehat{\beta}) = 0.21, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.20, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (0.99, 1.08), \text{median}(\widehat{\beta}, \widehat{\mu}) = (0.99, 1.00)$												
IF	91.05	94.05	98.00	1.55	1.84	2.42	0.94	1.12	1.47	1.73	2.06	2.70
HM	89.70	94.00	98.05	1.55	1.84	2.42	0.94	1.12	1.47	1.73	2.06	2.70
NB	92.30	94.95	98.00	8.59	10.23	13.45	1.11	1.33	1.74	8.34	9.94	13.06
PB	93.20	95.20	98.40	11.74	13.99	18.38	1.09	1.29	1.70	4.36	5.20	6.83
FI	89.70	95.25	99.05	∞	∞	∞	1.08	1.37	2.18	2.37	3.40	11.36
DIMER	90.05	95.30	99.00	1.91	2.70	16.91	1.08	1.37	2.14	2.34	3.26	7.92
LR Test	87.55	93.45	98.35	∞	∞	∞	1.01	1.27	1.97	2.17	3.03	7.91
INL–LR	0.6%	1.4%	6.3%									
INL–FI	0.6%	1.2%	5.5%									
$n = 50, \text{cv}(\widehat{\beta}) = 0.14, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (1.00, 1.02), \text{median}(\widehat{\beta}, \widehat{\mu}) = (0.99, 1.00)$												
IF	91.10	95.30	98.45	0.70	0.84	1.10	0.66	0.79	1.04	0.95	1.13	1.48
HM	90.60	95.80	98.60	0.70	0.84	1.10	0.66	0.79	1.04	0.95	1.13	1.48
NB	91.80	95.75	98.50	0.84	1.00	1.32	0.70	0.83	1.09	1.12	1.33	1.75
PB	93.05	96.90	98.70	0.78	0.93	1.22	0.71	0.84	1.11	1.07	1.28	1.68
FI	91.60	95.75	99.40	0.76	0.94	1.37	0.70	0.86	1.22	1.05	1.30	1.94
DIMER	91.65	95.70	99.40	0.76	0.94	1.36	0.71	0.86	1.21	1.05	1.30	1.93
LR Test	90.25	95.35	99.35	0.74	0.91	1.32	0.68	0.84	1.17	1.02	1.26	1.87
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.5: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (1.00, 1.00)$, where ϵ_i follows a normal distribution with mean 0, variance 1. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n=10, \mathrm{cv}(\widehat{\beta})=0.39, \mathrm{cv}(\widehat{\beta}\widehat{\mu})=-0.34, \rho(\widehat{\beta},\widehat{\beta}\widehat{\mu})=0.01$												
$\mathrm{mean}(\widehat{\beta},\widehat{\mu})=(0.99,-1.06), \mathrm{median}(\widehat{\beta},\widehat{\mu})=(1.01,-0.98)$												
IF	87.45	90.40	94.75	77.69	92.57	121.7	1.46	1.74	2.29	5.19	6.19	8.13
HM	81.95	87.80	93.20	77.69	92.57	121.7	1.46	1.74	2.29	5.19	6.19	8.13
NB	92.00	93.60	95.90	236.4	281.7	370.2	6.96	8.29	10.89	132.7	158.1	207.8
PB	90.40	92.90	95.30	193.3	230.4	302.7	3.80	4.53	5.95	129.3	154.1	202.6
FI	91.60	95.95	99.45	∞	∞	∞	2.35	3.76	∞	∞	∞	∞
DIMER	92.70	95.95	99.15	11.29	23.58	96.24	2.25	3.36	12.71	15.18	36.78	124.0
LR Test	85.70	91.80	97.55	∞	∞	∞	1.81	2.65	13.61	∞	∞	∞
INL–LR	16.1%	24.6%	49.5%									
INL–FI	20.4%	31.0%	59.5%									
$n=25, \mathrm{cv}(\widehat{\beta})=0.21, \mathrm{cv}(\widehat{\beta}\widehat{\mu})=-0.20, \rho(\widehat{\beta},\widehat{\beta}\widehat{\mu})=-0.01$												
$\mathrm{mean}(\widehat{\beta},\widehat{\mu})=(0.99,-1.08), \mathrm{median}(\widehat{\beta},\widehat{\mu})=(0.99,-1.01)$												
IF	89.45	93.75	97.60	1.68	2.00	2.62	0.94	1.12	1.47	1.66	1.98	2.60
HM	88.50	93.90	97.60	1.68	2.00	2.62	0.94	1.12	1.47	1.66	1.98	2.60
NB	91.95	95.00	97.90	9.57	11.40	14.98	1.09	1.30	1.71	7.37	8.78	11.53
PB	92.60	95.15	98.45	8.63	10.28	13.51	1.09	1.30	1.71	4.34	5.17	6.80
FI	89.90	95.05	99.20	∞	∞	∞	1.08	1.38	2.19	2.28	3.29	10.03
DIMER	90.35	94.95	99.10	1.92	2.71	17.66	1.08	1.37	2.15	2.24	3.17	7.57
LR Test	88.50	93.45	98.40	∞	∞	∞	1.01	1.27	1.98	2.08	2.93	7.09
INL–LR	0.6%	1.4%	6.5%									
INL–FI	0.6%	1.2%	5.5%									
$n=50, \mathrm{cv}(\widehat{\beta})=0.14, \mathrm{cv}(\widehat{\beta}\widehat{\mu})=-0.14, \rho(\widehat{\beta},\widehat{\beta}\widehat{\mu})=0.01$												
$\mathrm{mean}(\widehat{\beta},\widehat{\mu})=(1.00,-1.02), \mathrm{median}(\widehat{\beta},\widehat{\mu})=(0.99,-1.00)$												
IF	91.10	94.95	98.10	0.70	0.84	1.10	0.66	0.78	1.03	0.96	1.15	1.51
HM	90.90	95.15	98.30	0.70	0.84	1.10	0.66	0.78	1.03	0.96	1.15	1.51
NB	91.65	95.10	98.25	0.91	1.08	1.42	0.69	0.82	1.08	1.14	1.35	1.78
PB	93.10	95.65	98.55	0.78	0.93	1.22	0.70	0.83	1.10	1.09	1.30	1.71
FI	90.60	95.05	99.50	0.76	0.94	1.38	0.70	0.86	1.21	1.07	1.33	1.98
DIMER	90.65	95.00	99.40	0.76	0.94	1.36	0.70	0.85	1.20	1.07	1.33	1.97
LR Test	89.90	94.50	99.35	0.74	0.91	1.32	0.68	0.83	1.17	1.03	1.28	1.90
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.6: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i+\mu)+\epsilon_i$ with $(\beta,\mu) = (1.00,-1.00)$, where ϵ_i follows a normal distribution with mean 0, variance 1. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \text{cv}(\widehat{\beta}) = -0.38, \text{cv}(\widehat{\beta\mu}) = 0.34, \rho(\widehat{\beta}, \widehat{\beta\mu}) = 0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.01, -1.24), \text{median}(\widehat{\beta}, \widehat{\mu}) = (-0.99, -1.00)$												
IF	86.80	91.05	95.85	17.77	21.17	27.82	1.50	1.79	2.35	4.70	5.59	7.35
HM	83.20	89.85	94.60	17.77	21.17	27.82	1.50	1.79	2.35	4.70	5.59	7.35
NB	93.65	95.70	97.40	72.37	86.23	113.3	6.48	7.73	10.15	115.8	138.0	181.4
PB	91.40	93.65	96.30	103.7	123.6	162.4	4.05	4.83	6.34	137.7	164.1	215.7
FI	91.95	96.40	99.55	∞	∞	∞	2.44	4.01	∞	∞	∞	∞
DIMER	92.75	96.35	99.50	11.72	28.76	103.5	2.29	3.46	13.67	12.70	35.77	128.8
LR Test	85.25	91.60	97.75	∞	∞	∞	1.86	2.73	16.28	∞	∞	∞
INL–LR	14.8%	24.1%	49.9%									
INL–FI	18.9%	30.4%	59.8%									
$n = 25, \text{cv}(\widehat{\beta}) = -0.21, \text{cv}(\widehat{\beta\mu}) = 0.20, \rho(\widehat{\beta}, \widehat{\beta\mu}) = -0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.01, -1.05), \text{median}(\widehat{\beta}, \widehat{\mu}) = (-1.01, -0.99)$												
IF	90.20	93.90	97.00	1.06	1.27	1.66	0.92	1.10	1.44	1.63	1.95	2.56
HM	89.60	94.35	97.15	1.06	1.27	1.66	0.92	1.10	1.44	1.63	1.95	2.56
NB	92.00	94.60	97.25	46.90	55.88	73.44	1.12	1.33	1.75	6.42	7.65	10.06
PB	92.85	95.30	97.60	5.22	6.22	8.18	1.07	1.28	1.68	3.69	4.39	5.77
FI	89.60	94.75	98.95	∞	∞	∞	1.06	1.34	2.13	2.25	3.22	9.04
DIMER	90.05	94.85	98.95	1.35	1.95	5.82	1.06	1.33	2.09	2.21	3.09	7.18
LR Test	88.40	93.35	98.25	∞	∞	∞	0.99	1.24	1.93	2.07	2.87	6.92
INL–LR	0.2%	1.0%	5.4%									
INL–FI	0.2%	0.9%	4.5%									
$n = 10, \text{cv}(\widehat{\beta}) = -0.14, \text{cv}(\widehat{\beta\mu}) = 0.14, \rho(\widehat{\beta}, \widehat{\beta\mu}) = 0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.00, -1.02), \text{median}(\widehat{\beta}, \widehat{\mu}) = (-1.01, -1.00)$												
IF	90.50	95.15	98.65	0.70	0.84	1.10	0.65	0.77	1.02	0.98	1.17	1.53
HM	90.10	95.50	98.90	0.70	0.84	1.10	0.65	0.77	1.02	0.98	1.17	1.53
NB	91.95	95.30	98.65	0.88	1.05	1.38	0.69	0.82	1.08	1.17	1.40	1.84
PB	92.40	96.30	99.15	0.81	0.97	1.27	0.69	0.83	1.09	1.11	1.33	1.75
FI	90.60	95.05	99.50	0.76	0.94	∞	0.69	0.85	1.20	1.09	1.36	2.04
DIMER	90.65	94.95	99.40	0.76	0.94	1.38	0.69	0.85	1.19	1.09	1.36	2.03
LR Test	89.90	94.50	99.35	0.74	0.91	∞	0.67	0.82	1.16	1.06	1.32	1.95
INL–LR	0.0%	0.0%	0.1%									
INL–FI	0.0%	0.0%	0.1%									

Table S.7: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (-1.00, -1.00)$, where ϵ_i follows a normal distribution with mean 0, variance 1. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \text{cv}(\widehat{\beta}) = 0.38, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.35, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.02$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (1.01, -0.03), \text{median}(\widehat{\beta}, \widehat{\mu}) = (1.00, 0.95)$												
IF	85.15	88.45	92.95	3732	4446	5844	1.41	1.68	2.21	4.90	5.83	7.67
HM	80.70	85.55	91.85	3732	4446	5844	1.41	1.68	2.21	4.90	5.83	7.67
NB	89.60	91.50	94.75	436.7	520.4	683.9	6.35	7.57	9.94	139.2	165.8	218.0
PB	88.15	90.45	94.60	116.0	138.2	181.6	3.25	3.88	5.09	131.9	157.1	206.5
FI	90.20	95.05	99.05	∞	∞	∞	2.23	3.62	∞	∞	∞	∞
DIMER	90.85	94.95	98.95	14.67	27.01	86.81	2.15	3.20	11.73	13.80	36.35	118.2
LR Test	83.35	89.75	97.50	∞	∞	∞	1.74	2.47	9.18	∞	∞	∞
INL–LR	15.0%	23.8%	46.6%									
INL–FI	19.2%	30.3%	56.0%									
$n = 25, \text{cv}(\widehat{\beta}) = 0.21, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.21, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (1.01, 1.06), \text{median}(\widehat{\beta}, \widehat{\mu}) = (1.01, 0.98)$												
IF	89.40	93.10	96.50	1.12	1.34	1.76	0.92	1.10	1.44	1.72	2.05	2.69
HM	88.30	93.35	96.80	1.12	1.34	1.76	0.92	1.10	1.44	1.72	2.05	2.69
NB	89.95	93.10	96.50	21.90	26.10	34.30	1.11	1.32	1.74	8.20	9.77	12.84
PB	91.80	94.60	97.25	89.62	106.8	140.4	1.07	1.27	1.67	4.15	4.94	6.49
FI	89.55	94.85	98.70	∞	∞	∞	1.06	1.35	2.15	2.40	3.47	11.67
DIMER	89.90	94.90	98.60	1.93	2.68	9.65	1.07	1.35	2.11	2.36	3.31	8.08
LR Test	87.50	93.10	97.90	∞	∞	∞	0.99	1.25	1.94	2.19	3.06	8.09
INL–LR	0.5%	1.5%	6.3%									
INL–FI	0.4%	1.4%	5.5%									
$n = 50, \text{cv}(\widehat{\beta}) = 0.14, \text{cv}(\widehat{\beta}\widehat{\mu}) = 0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.02$												
$\text{mean}(\widehat{\beta}, \widehat{\mu}) = (1.00, 1.02), \text{median}(\widehat{\beta}, \widehat{\mu}) = (1.00, 0.99)$												
IF	91.65	94.90	98.00	0.70	0.84	1.10	0.65	0.77	1.02	0.99	1.17	1.54
HM	91.25	95.00	98.05	0.70	0.84	1.10	0.65	0.77	1.02	0.99	1.17	1.54
NB	91.80	94.75	97.35	1.02	1.21	1.59	0.69	0.82	1.08	1.25	1.49	1.95
PB	93.20	96.00	98.40	0.82	0.97	1.28	0.69	0.82	1.08	1.12	1.33	1.75
FI	90.70	95.50	98.85	0.76	0.94	1.39	0.69	0.85	1.19	1.10	1.37	2.07
DIMER	90.70	95.40	98.85	0.76	0.94	1.37	0.69	0.84	1.18	1.10	1.37	2.05
LR Test	90.00	94.90	98.75	0.74	0.91	1.33	0.67	0.82	1.15	1.06	1.32	1.97
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.8: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (1.00, 1.00)$, where ϵ_i follows a skewed normal distribution with mean 0, variance 1 and skewness 0.78. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \mathrm{cv}(\widehat{\beta}) = 0.38, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.35, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (1.01, -0.20), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (1.00, -1.02)$												
IF	87.50	91.05	96.00	2979	3550	4666	1.45	1.73	2.28	4.48	5.33	7.01
HM	82.50	89.00	94.70	2979	3550	4666	1.45	1.73	2.28	4.48	5.33	7.01
NB	93.30	95.30	97.10	219.5	261.5	343.7	5.78	6.88	9.05	96.77	115.3	151.5
PB	91.50	94.10	96.85	167.8	199.9	262.7	3.41	4.06	5.34	103.6	123.4	162.2
FI	90.95	95.70	99.10	∞	∞	∞	2.28	3.53	∞	∞	∞	∞
DIMER	91.75	96.00	99.10	9.66	22.14	72.72	2.23	3.33	12.07	11.93	29.91	102.9
LR Test	84.25	91.55	97.75	∞	∞	∞	1.81	2.61	9.70	∞	∞	∞
INL–LR	14.8%	23.6%	46.6%									
INL–FI	19.2%	30.3%	56.0%									
$n = 25, \mathrm{cv}(\widehat{\beta}) = 0.21, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.21, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (1.01, -1.04), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (1.01, -0.99)$												
IF	89.45	93.80	97.35	1.09	1.30	1.70	0.92	1.10	1.45	1.63	1.94	2.55
HM	88.95	94.25	97.50	1.09	1.30	1.70	0.92	1.10	1.45	1.63	1.94	2.55
NB	91.95	95.65	98.00	21.58	25.72	33.80	1.07	1.28	1.68	6.28	7.48	9.84
PB	92.05	95.00	98.05	96.37	114.8	150.9	1.06	1.26	1.66	3.94	4.70	6.18
FI	89.90	94.55	99.05	∞	∞	∞	1.06	1.34	2.12	2.23	3.26	9.69
DIMER	90.20	94.65	99.00	1.65	2.34	8.49	1.06	1.34	2.09	2.18	3.08	7.34
LR Test	88.40	93.05	98.20	∞	∞	∞	0.99	1.25	1.93	2.04	2.87	7.06
INL–LR	0.5%	1.4%	6.3%									
INL–FI	0.4%	1.4%	5.5%									
$n = 50, \mathrm{cv}(\widehat{\beta}) = 0.14, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = -0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (1.00, -1.02), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (1.00, -1.00)$												
IF	90.00	94.45	98.65	0.70	0.83	1.09	0.66	0.78	1.03	0.96	1.14	1.50
HM	89.15	94.00	98.85	0.70	0.83	1.09	0.66	0.78	1.03	0.96	1.14	1.50
NB	90.10	94.80	98.80	0.85	1.02	1.34	0.68	0.81	1.07	1.06	1.27	1.67
PB	91.65	95.50	99.15	0.80	0.95	1.25	0.70	0.83	1.09	1.10	1.31	1.72
FI	89.50	94.60	98.75	0.76	0.93	1.37	0.70	0.86	1.21	1.07	1.34	2.01
DIMER	89.55	94.55	98.65	0.76	0.93	1.35	0.70	0.85	1.20	1.07	1.33	1.99
LR Test	88.85	94.05	98.50	0.73	0.90	1.31	0.68	0.83	1.17	1.04	1.29	1.92
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.9: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (1.00, -1.00)$, where ϵ_i follows a skewed normal distribution with mean 0, variance 1 and skewness 0.78. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.

	Mean of Coverage			Mean of Length			Median of Length			90% Quantile of Length		
Method	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI	90% CI	95% CI	99% CI
$n = 10, \mathrm{cv}(\widehat{\beta}) = -0.38, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = 0.35, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = -0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-0.99, -1.23), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.00, -0.96)$												
IF	86.70	89.75	94.40	10.70	12.74	16.75	1.42	1.69	2.23	5.62	6.70	8.80
HM	81.10	86.75	92.65	10.70	12.74	16.75	1.42	1.69	2.23	5.62	6.70	8.80
NB	90.65	92.40	95.10	147.5	175.8	231.0	6.54	7.80	10.25	141.0	168.0	220.8
PB	88.95	91.40	95.00	257.3	306.5	402.9	3.79	4.52	5.94	151.1	180.1	236.7
FI	91.90	96.15	99.10	∞	∞	∞	2.31	3.81	∞	∞	∞	∞
DIMER	92.60	96.15	99.05	10.13	19.19	75.70	2.18	3.34	12.58	16.73	41.77	120.1
LR Test	85.00	92.10	98.00	∞	∞	∞	1.77	2.59	11.24	∞	∞	∞
INL–LR	16.9%	24.8%	48.5%									
INL–FI	21.0%	30.5%	57.1%									
$n = 25, \mathrm{cv}(\widehat{\beta}) = -0.22, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = 0.21, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.01$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-0.99, -1.07), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-0.99, -1.01)$												
IF	90.65	93.85	96.90	1.14	1.36	1.79	0.93	1.11	1.46	1.79	2.13	2.80
HM	90.10	94.15	97.20	1.14	1.36	1.79	0.93	1.11	1.46	1.79	2.13	2.80
NB	91.65	93.90	96.55	17.11	20.39	26.80	1.14	1.35	1.78	11.87	14.14	18.59
PB	92.90	95.00	97.60	19.52	23.26	30.57	1.08	1.29	1.70	5.15	6.13	8.06
FI	90.15	94.85	99.10	∞	∞	∞	1.08	1.37	2.17	2.45	3.54	12.09
DIMER	90.80	95.20	99.10	1.71	5.60	13.56	1.08	1.37	2.13	2.40	3.41	8.43
LR Test	88.35	93.05	98.20	∞	∞	∞	1.01	1.27	1.96	2.23	3.13	8.33
INL–LR	0.7%	1.7%	7.0%									
INL–FI	0.7%	1.6%	6.2%									
$n = 50, \mathrm{cv}(\widehat{\beta}) = -0.14, \mathrm{cv}(\widehat{\beta}\widehat{\mu}) = 0.14, \rho(\widehat{\beta}, \widehat{\beta}\widehat{\mu}) = 0.02$												
$\mathrm{mean}(\widehat{\beta}, \widehat{\mu}) = (-1.00, -1.02), \mathrm{median}(\widehat{\beta}, \widehat{\mu}) = (-1.00, -1.00)$												
IF	90.50	94.40	97.40	0.70	0.83	1.10	0.65	0.78	1.02	0.98	1.17	1.54
HM	89.80	94.80	97.60	0.70	0.83	1.10	0.65	0.78	1.02	0.98	1.17	1.54
NB	90.35	93.90	97.15	0.90	1.07	1.41	0.69	0.83	1.09	1.23	1.46	1.92
PB	92.30	95.25	97.80	0.78	0.93	1.22	0.69	0.83	1.09	1.13	1.35	1.77
FI	89.50	94.60	98.75	0.76	0.94	1.37	0.69	0.85	1.20	1.09	1.36	2.05
DIMER	89.55	94.55	98.65	0.76	0.94	1.36	0.69	0.85	1.19	1.09	1.36	2.03
LR Test	88.85	94.05	98.50	0.74	0.91	1.32	0.67	0.82	1.16	1.06	1.32	1.96
INL–LR	0.0%	0.0%	0.0%									
INL–FI	0.0%	0.0%	0.0%									

Table S.10: Confidence intervals for μ in a simulation study with 2000 replications for linear regression model $Y_i = \beta(X_i + \mu) + \epsilon_i$ with $(\beta, \mu) = (-1.00, -1.00)$, where ϵ_i follows a skewed normal distribution with mean 0, variance 1 and skewness 0.78. "INL–LR" depicts the % of times that the interval by the likelihood ratio test was of infinite length, and "INL–FI" depicts the % of times that Fieller's interval was infinite length, either the entire real line or two infinite length disconnected intervals. Here the acronyms are IF–Inverse Fisher score method, HM–Hayya's Method, NB–Nonparametric Bootstrap, PB–Parametric Bootstrap, FI–Fieller's Interval, DIMER–Direct Integral Method for Ratios and LR Test—Likelihood ratio test.