**Supplementary table 1 and 2:** The average coverage of estimated CIs for the RI limits and average CI width across integer age and sex for Hoq *et al* and Royston’s method **(**Monsurul Hoq Susan Donath,Paul Monagle, John B. Carlin Comparison of statistical methods for estimating continuous paediatric reference intervals: a simulation study)

**Table S-1**: Average coverage across integer age and sex for Hoq *et al* and Royston’s methods, for five scenarios and four sample sizes

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Performance Measure | | Coverage | | | | | | | | | | | | |
| Limit | | **Lower limit** | | | | | |  | **Upper limit** | | | | | |
| Sample size | | **100** | **200** | | **400** | | **1000** |  | **100** | **200** | **400** | | **1000** |
| Scenario | **Method** |  |  | |  | |  |  |  |  |  | |  |
| 1a | Hoq *et al* | 63.0 | 84.1 | **93.8** | | **93.9** | |  | 65.3 | 83.5 | **95.0** | **93.4** | |
| Royston | 84.5 | 87.8 | 83.7 | | 65.6 | | 66.0 | 60.4 | 47.9 | 25.5 | |
| 2b | Hoq *et al* | 58.4 | 81.7 | **95.1** | | **95.5** | |  | 49.4 | 79.6 | **95.1** | **94.5** | |
| Royston | 76.3 | 74.4 | 81.4 | | 86.1 | |  | 63.6 | 69.4 | 72.5 | 67.8 | |
| 3c | Hoq *et al* | 79.7 | **94.7** | **95.1** | | **95.7** | |  | 79.4 | **95.3** | **95.0** | **95.9** | |
| Royston | **85.1** | **85.0** | **89.4** | | **90.5** | |  | **85.5** | **89.1** | **89.1** | **91.5** | |
| 4d | Hoq *et al* | 77.1 | **92.7** | 88.4 | | 77.3 | |  | 76.2 | **90.8** | 87.2 | 70.9 | |
| Royston | 76.3 | 84.0 | 83.4 | | 75.3 | | 73.8 | 76.0 | 73.6 | 60.3 | |
| 5e | Hoq *et al* | 68.6 | 87.4 | 84.5 | | 67.2 | |  | 68.2 | 83.4 | 82.1 | 67.1 | |
| Royston | 69.5 | 63.7 | 49.5 | | 30.6 | |  | 70.0 | 61.5 | 49.3 | 34.7 | |

Coverage more than 90% are highlighted with bold font.

1. Linear in age (separately by sex), SD increasing linearly with age e.g. Creatinine.
2. Nonlinear in age (separately by sex), SD increasing nonlinearly with age e.g. Alkaline Phosphatase.
3. Linear in age, constant variance, no sex difference e.g. Potassium.
4. Nonlinear in age, SD increasing linearly with age, sex difference e.g. Total Protein.
5. Nonlinear in age, constant variance, no sex difference e.g. Phosphate.

**Table S-2**: Average 95% confidence interval width for lower and upper reference limits for Hoq *et al* and Royston’s methods across integer age and sex, for five scenarios and four sample sizes

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Performance Measure | | Average confidence interval width | | | | | | | | | | | |
| Limit | | **Lower limit** | | | | | |  | **Upper limit** | | | | |
| Sample size | | **100** | **200** | | **400** | | **1000** |  | **100** | **200** | **400** | | **1000** |
| Scenario | **Method** |  |  | |  | |  |  |  |  |  | |  |
| 1a | Hoq *et al* | 7.6 | 8.8 | 8.6 | | 5.0 | |  | 8.0 | 8.6 | 8.6 | 4.9 | |
| **Royston** | 8.3 | **6.2** | **4.4** | | **2.8** | | 8.3 | **6.2** | **4.4** | **2.8** | |
| 2b | Hoq *et al* | 58.9 | 74.9 | 81.7 | | 49.2 | |  | 69.5 | 81.3 | 88.3 | 52.8 | |
| Royston | 68.3 | **55.2** | **42.1** | | **27.3** | |  | **75.0** | **57.7** | **43.0** | **27.4** | |
| 3c | Hoq *et al* | 0.35 | 0.38 | 0.26 | | 0.15 | |  | 0.35 | 0.39 | 0.26 | 0.15 | |
| **Royston** | **0.22** | **0.16** | **0.12** | | **0.08** | |  | **0.22** | **0.16** | **0.12** | **0.08** | |
| 4d | Hoq *et al* | 5.17 | 5.72 | 3.61 | | 2.18 | |  | 5.11 | 5.48 | 3.54 | 2.15 | |
| **Royston** | **3.73** | **2.76** | **1.98** | | **1.25** | |  | **3.75** | **2.75** | **1.98** | **1.25** | |
| 5e | Hoq *et al* | 0.17 | 0.20 | 0.14 | | 0.09 | |  | 0.18 | 0.19 | 0.14 | 0.08 | |
| **Royston** | **0.13** | **0.09** | **0.07** | | **0.04** | |  | **0.13** | **0.09** | **0.07** | **0.04** | |

Lowest confidence interval width between Hoq et al and Royston’s method was highlighted with bold font.

1. Linear in age (separately by sex), SD increasing linearly with age e.g. Creatinine.
2. Nonlinear in age (separately by sex), SD increasing nonlinearly with age e.g. Alkaline Phosphatase.
3. Linear in age, constant variance, no sex difference e.g. Potassium.
4. Nonlinear in age, SD increasing linearly with age, sex difference e.g. Total Protein.
5. Nonlinear in age, constant variance, no sex difference e.g. Phosphate.