A novel method for creatinine adjustment makes the revised Lund-Malmö GFR estimating equation applicable in children

Supplementary material

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Figure S1 Median creatinine values in the Kortrijk (n=9 634), Liege (9 123) and Uppsala (n=64 410) cohorts in A) females and B) males.

Table S1 Measurement procedures used in the included cohorts

Table S2 Age and sex specific reference intervals for creatinine in Kortrijk, Liege and Uppsala in comparison with the estimated geometric means from the creatinine growth curves.

Table S3 Bias and accuracy of GFR equations stratified by measured glomerular filtration rate.

Table S4A Bias and accuracy of GFR equations stratified by age and measured glomerular filtration rate <75 mL/min/1.73 m²

Table S4B Bias and P₃₀ accuracy of GFR equations stratified by age and measured glomerular filtration rate ≥75 mL/min/1.73 m²

Table S5A Bias and accuracy of GFR equations stratified by cohort and measured glomerular filtration rate <75 mL/min/1.73 m²

Table S5B Bias and P₃₀ accuracy of GFR equations stratified by cohort and measured glomerular filtration rate ≥75 mL/min/1.73 m²
| Origin, time of collection | Number (%) | Creatinine assay | Clearance method |
|---------------------------|------------|------------------|------------------|
| Amsterdam (Netherlands), 2004-2012 [1-3] | 399 (10) | Abbott enzymatic, Roche enzymatic | Inulin 4-points plasma clearance at 10, 30, 90 and 240 minutes |
| Leuven (Belgium), 2012-2015 [4] | 421 (11) | Creatinine Plus, Roche enzymatic | $^{51}$Cr-EDTA 4-points plasma clearance at 60, 120, 180 and 240 minutes |
| Lund (Sweden), 2008-2010 [5, 6] | 434 (11) | Abbott enzymatic | Iohexol 1-point* ($\geq 40$ kg) and 2-points* ($<40$ kg) plasma clearance |
| Lyon (France), 2003-2011 [7] | 1459 (36) | Jaffe before 2010, then Creatinine Plus, Roche enzymatic | Inulin renal clearance or iohexol 3-points plasma clearance at 120, 180 and 240 minutes, if eGFR <30 $4^{th}$ point at 360 min |
| Stockholm (Sweden), 2011-2016 [6] | 1284 (32) | Creatinine Plus, Roche enzymatic or Beckman-Coulter Jaffe | Iohexol 4-points* plasma clearance |
| Örebro (Sweden), 2004-2017 [8, 9] | 8 (0.2) | Roche enzymatic and Ortho Clinical Diagnostics enzymatic | Iohexol 1-point* plasma clearance |

An external quality assessment system was provided by Equalis AB (Uppsala, Sweden, www.equalis.se/en) for the iohexol measurements in Lund, Lyon, Stockholm and Örebro.

*Blood sampling time was based on estimated GFR or plasma/serum creatinine values.
Table S2. Age and sex specific reference intervals for serum creatinine concentrations (µmol/L) in Kortrijk, Liège and Uppsala in comparison with the estimated geometric means from the creatinine growth curves.

| Age (years) | Kortrijk | Liège | Uppsala | Growth Curve | Kortrijk | Liège | Uppsala | Growth Curve |
|-------------|----------|-------|---------|--------------|----------|-------|---------|--------------|
|             | Females  |       |         |              | Males    |       |         |              |
| 2<3         | 15-35    | 18-38 | 22-53   | 26           | 15-35    | 18-38 | 22-53   | 27           |
| 3<4         | 18-38    | 18-38 | 22-53   | 28           | 18-38    | 18-38 | 22-53   | 27           |
| 4<5         | 20-42    | 18-48 | 22-53   | 30           | 20-42    | 18-48 | 22-53   | 29           |
| 5<6         | 21-44    | 27-54 | 22-53   | 32           | 21-44    | 27-54 | 22-53   | 31           |
| 6<7         | 25-49    | 27-54 | 31-70   | 35           | 25-49    | 27-54 | 31-76   | 34           |
| 7<8         | 26-51    | 27-54 | 31-70   | 37           | 26-51    | 27-54 | 31-76   | 37           |
| 8<9         | 27-54    | 27-54 | 31-70   | 40           | 27-54    | 27-54 | 31-76   | 40           |
| 9<10        | 27-57    | 27-54 | 31-70   | 43           | 27-57    | 27-54 | 31-76   | 44           |
| 10<11       | 31-59    | 27-54 | 31-70   | 45           | 31-59    | 27-54 | 31-76   | 47           |
| 11<12       | 31-62    | 27-54 | 36-70   | 48           | 31-62    | 27-54 | 44-90   | 51           |
| 12<13       | 34-66    | 40-72 | 36-70   | 50           | 34-66    | 40-72 | 44-90   | 54           |
| 13<14       | 34-72    | 40-72 | 36-70   | 52           | 34-72    | 40-72 | 44-90   | 58           |
| 14<15       | 37-72    | 40-72 | 36-70   | 54           | 41-77    | 40-72 | 44-90   | 61           |
| 15<16       | 42-75    | 43-74 | 49-86   | 56           | 45-90    | 55-95 | 55-106  | 64           |
| 16<17       | 42-80    | 43-74 | 49-86   | 57           | 48-94    | 55-95 | 55-106  | 67           |
| 17<18       | 44-80    | 43-74 | 49-86   | 59           | 54-94    | 55-95 | 55-106  | 70           |
| 18-40       | 44-82    | 49-90 | 45-90   | 62*          | 57-100   | 65-104| 60-105  | 79*          |

*Mean value across the estimates for the age interval 18-40 years.
| mGFR intervals | N (%) | CKiD | Schwartz-Lyon | LMR | LMR18 |
|----------------|-------|------|---------------|-----|-------|
| Bias           |       |      |               |     |       |
| <30            | 95 (2.4) | 5.7  | 2.8           | 6.1 | 0.9   |
| 30-44          | 134 (3.3) | 6.4  | 2.7           | 15.1 | 1.8 |
| 45-59          | 264 (6.6) | 6.9  | 2.2           | 15.2 | 4.3 |
| 60-74          | 439 (11) | 8.1  | 2.1           | 15.4 | 6.9 |
| 75-89          | 679 (17) | 6.3  | -0.4          | 9.3  | 3.2 |
| 90-119         | 1606 (40) | 3.6  | -5.2          | -2.8 | -6.2 |
| ≥120           | 788 (20) | -0.4 | -14.1         | -27.4 | -27.3 |
| P_{30} (%)     |       |      |               |     |       |
| <30            | 51    | 56   | 49            | 61  |       |
| 30-44          | 65    | 74   | 40            | 64  |       |
| 45-59          | 75    | 86   | 52            | 75  |       |
| 60-74          | 76    | 85   | 64            | 80  |       |
| 75-89          | 79    | 87   | 87            | 90  |       |
| 90-119         | 83    | 88   | 96            | 95  |       |
| ≥120           | 84    | 84   | 77            | 80  |       |

Median bias (eGFR-mGFR) expressed in mL/min/1.73 m² and accuracy in percentage of GFR estimates within ±30% of mGFR (P_{30}). CKiD = Chronic Kidney Disease in Children, LMR = Lund-Malmö revised, LMR18 = LMR based on creatinine values adjusted to age 18 years, eGFR = estimated glomerular filtration rate, mGFR = measured GFR.
Table S4A. Median bias and accuracy ($P_{30}$) of GFR estimating equations stratified by age and measured glomerular filtration rate (mGFR) <75 mL/min/1.73 m$^2$ in children (n=932).

| Age intervals (years) | N (%)  | Median mGFR | CKiD | Schwartz-Lyon | LMR  | LMR18 |
|-----------------------|--------|-------------|------|--------------|------|-------|
| Bias                  |        |             |      |              |      |       |
| 2.0-7.9               | 211 (23)| 57          | 12.4 | 5.8          | 17.8 | 2.1   |
| 8.0-12.9              | 262 (28)| 58          | 7.3  | 1.2          | 17.7 | 4.7   |
| 13.0-17.9             | 459 (49)| 59          | 4.7  | 1.8          | 10.0 | 6.3   |
| $P_{30}$ (%)          |        |             |      |              |      |       |
| 2.0-7.9               |        | 61          | 72   | 46           | 72   |       |
| 8.0-12.9              |        | 74          | 87   | 47           | 79   |       |
| 13.0-17.9             |        | 76          | 81   | 65           | 73   |       |

Median bias (eGFR-mGFR) expressed in mL/min/1.73 m$^2$ and accuracy in percentage of GFR estimates within ±30% of mGFR ($P_{30}$). CKiD = Chronic Kidney Disease in Children, LMR = Lund-Malmö revised, LMR18 = LMR based on creatinine values adjusted to age 18 years, eGFR = estimated glomerular filtration rate, mGFR = measured GFR.
| Age intervals (years) | N (%) | Median mGFR | CKiD | Schwartz-Lyon | LMR | LMR18 |
|-----------------------|-------|-------------|------|---------------|-----|-------|
| Bias                  | N (%) | Median mGFR | CKiD | Schwartz-Lyon | LMR | LMR18 |
| 2.0-7.9               | 839 (15) | 111 | 12.6 | -0.5 | -16.7 | -15.7 |
| 8.0-12.9              | 882 (16) | 105 | 6.8  | -5.6 | 0.9  | -6.3  |
| 13.0-17.9             | 1352 (25) | 101 | -3.4 | -7.7 | -3.2 | -5.8  |
| $P_{30}$ (%)          | N (%) |Median bias  |    |               |     |       |
| 2.0-7.9               | 74    | 83  | 79  | 82  |
| 8.0-12.9              | 86    | 91  | 93  | 94  |
| 13.0-17.9             | 85    | 86  | 92  | 93  |

Median bias (eGFR-mGFR) expressed in mL/min/1.73 m² and accuracy in percentage of GFR estimates within ±30% of mGFR ($P_{30}$). CKiD = Chronic Kidney Disease in Children, LMR = Lund-Malmö revised, LMR18 = LMR based on creatinine values adjusted to age 18 years, eGFR = estimated glomerular filtration rate, mGFR = measured GFR.
**Table S5A.** Median bias and accuracy (P$_{30}$) of GFR estimating equations stratified by cohorts and measured glomerular filtration rate (mGFR) <75 mL/min/1.73 m$^2$ in children (n=932).

| Age intervals (years) | N (%) | CKiD | Schwartz-Lyon | LMR | LMR18 |
|-----------------------|-------|------|---------------|-----|-------|
| Bias                  |       |      |               |     |       |
| Amsterdam             | 106 (11) | 3.5  | -0.8          | 9.1 | 2.2   |
| Leuven                | 106 (11) | 8.2  | 3.3           | 13.5| 3.5   |
| Lund                  | 89 (10)  | 7.4  | 4.2           | 13.9| 2.2   |
| Lyon                  | 400 (43) | 7.0  | 2.1           | 16.1| 6.3   |
| Stockholm             | 229 (25) | 8.5  | 3.3           | 14.3| 4.3   |
| Örebro                | 2 (0.2)     | NA   | NA            | NA  | NA    |
| P$_{30}$ (%)          |       |      |               |     |       |
| Amsterdam             | 76    | 78   | 66            | 74  |
| Leuven                | 70    | 78   | 55            | 74  |
| Lund                  | 63    | 70   | 51            | 71  |
| Lyon                  | 75    | 86   | 53            | 76  |
| Stockholm             | 68    | 78   | 58            | 74  |
| Örebro                | NA    | NA   | NA            | NA  |

Median bias (eGFR-mGFR) expressed in mL/min/1.73 m$^2$ and accuracy in percentage of GFR estimates within ±30% of mGFR (P$_{30}$). CKiD = Chronic Kidney Disease in Children, LMR = Lund-Malmö revised, LMR18 = LMR based on creatinine values adjusted to age 18 years, eGFR = estimated glomerular filtration rate, mGFR = measured GFR.
Table S5B. Median bias and accuracy ($P_{30}$) of GFR estimating equations stratified by cohorts and measured glomerular filtration rate (mGFR) $\geq$75 mL/min/1.73 m$^2$ in children (n=3 073).  

| Age intervals (years) | N (%) | CKiD | Schwartz-Lyon | LMR | LMR18 |
|-----------------------|-------|------|---------------|-----|-------|
| Bias                  |       |      |               |     |       |
| Amsterdam             | 293 (10) | 7.1  | -1.3          | -2.0 | -5.3  |
| Leuven                | 315 (10) | 8.4  | -0.5          | -2.3 | -5.2  |
| Lund                  | 345 (11) | 2.9  | -6.6          | -11.4 | -13.8 |
| Lyon                  | 1059 (34) | 1.3  | -7.9          | -3.1 | -8.4  |
| Stockholm             | 1055 (34) | 4.7  | -3.8          | -6.5 | -8.0  |
| Örebro                | 6 (0.2) | NA   | NA            | NA  | NA    |
| $P_{30}$ (%)          |       |      |               |     |       |
| Amsterdam             | 76    | 80   | 90            | 90  | 90    |
| Leuven                | 67    | 71   | 84            | 80  | 80    |
| Lund                  | 79    | 83   | 79            | 81  |       |
| Lyon                  | 90    | 93   | 94            | 94  |       |
| Stockholm             | 82    | 88   | 89            | 93  |       |
| Örebro                | NA    | NA   | NA            | NA  | NA    |

Median bias (eGFR-mGFR) expressed in mL/min/1.73 m$^2$ and accuracy in percentage of GFR estimates within $\pm$30% of mGFR ($P_{30}$). CKiD = Chronic Kidney Disease in Children, LMR = Lund-Malmö revised, LMR18 = LMR based on creatinine values adjusted to age 18 years, eGFR = estimated glomerular filtration rate, mGFR = measured GFR.
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