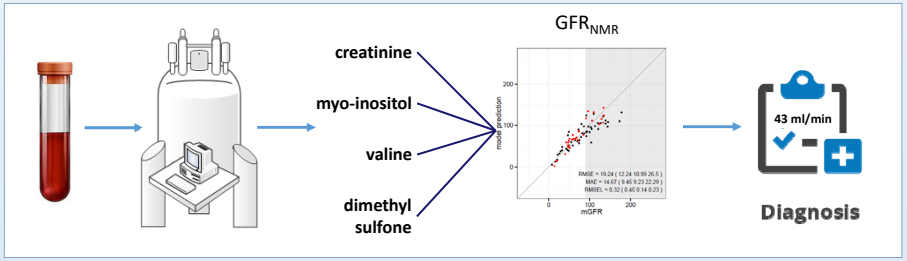
# NOVEL NMR-BASED METHOD FOR PREDICTION OF GLOMERULAR FILTRATION RATE PERFORMS WELL IN CHILDREN

*Jochen Ehrich[1], Laurence Dubourg[2], Sverker Hansson[3], Jens Drube[1], Lars Pape[1], Katharina Schäffler[4], Tobias Steinle[4], Jana Fruth[4], Sebastian Höckner[4], Eric Schiffer[4]*

*[1]Children's Hospital, Hannover Medical School, Hannover, Germany, [2]Service d'Explorations Fonctionnelles Rénales et Métaboliques, Hôpital Edouard Herriot, Lyon, France, [3]Department of Pediatrics, Sahlgrenska University Hospital, Gothenburg, Sweden, [4]numares AG, Regensburg, Germany*

## BACKGROUND

Creatinine based estimation of glomerular filtration rate ($eGFR_{creat}$) in children requires different equations than in adults. Different pediatric equations have been established; however, these equations still show suboptimal performances in the upper and lower GFR range. Recently, a novel serum-based method for accurate prediction of GFR using a nuclear magnetic resonance ($GFR_{NMR}$) spectroscopy-based biomarker constellation (creatinine, myo-inositol, valine, and dimethyl sulfone) was developed. This method outperformed the conventional eGFR equations when validated in three separate cohorts of predominantly adult patients. In this study, we evaluate the performance of $GFR_{NMR}$ in a pediatric cohort.




## METHODS

The value of the $GFR_{NMR}$ in children was investigated by testing its performance in a cohort of 77 children (40 girls, 37 boys) aged between 3 and 18 years. The NMR-based method was compared to $eGFR_{creat}$ obtained by the updated "Bedside" Schwartz formula.

| | cohort |
|---|---|
| **n** | 77 |
| **Age (range)** | 2.9 – 17.9 |
| **Sex (girls / boys)** | 40 / 37 |
| **CKD stage (1 / 2 / 3 / 4 / 5)** | 37 / 16 / 19 / 4 / 1 |
| **mGFR** | |
| **$^{51}$Cr-EDTA** | 44 |
| **Iohexol** | 33 |

In addition, the cystatin C-based equation derived from the CKiD cohort was used for calculating cystatin C-based eGFR (eGFRcys). Pearson correlation coefficient (r) with 95 % confidence interval, root mean square error (RMSE), and the percentage of eGFR values within 30% of measured GFR (P30) were calculated to assess the accuracy of the methods.

## CONTACT DETAILS

maulik.shah@numares.com

**Follow numares:** @numares AG @numares AG @Agnumares

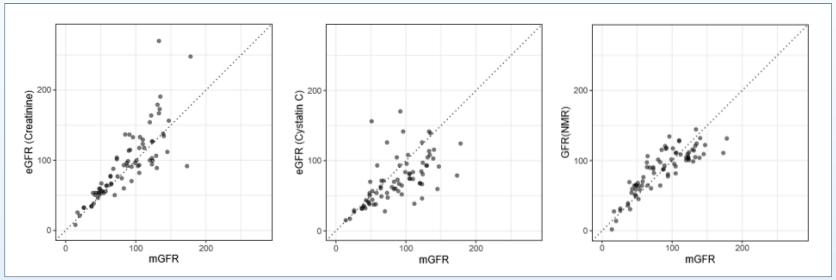
## RESULTS

In a cohort comprising pediatric patients with various degrees of kidney impairment covering the whole GFR range, the NMR-based method showed a higher correlation with mGFR compared to $eGFR_{creat}$ (r=0.85 vs. r=0.80).

Moreover, the RMSE was reduced from 28.4 for $eGFR_{creat}$ and 34.8 for $eGFR_{cys}$ to 20.0 for $GFR_{NMR}$. The NMR biomarker constellation also showed a higher accuracy in mGFR prediction with a P30 of 79.0% compared to 67.0% for $eGFR_{cys}$ and a similar P30 of 79.0% for $eGFR_{creat}$.

We tested in multivariate variance analysis whether the NMR approach allows accurate estimation of GFR independent of underlying renal etiology. We categorized observed etiologies as either glomerular (n=19), tubolo-interstitial (n=30) or mixed (n=28) renal dysfunction.

While $GFR_{NMR}$ was a highly significant predictor of mGFR, renal dysfunction did not impact the accuracy of $GFR_{NMR}$.




| | $eGFR_{creat}$ | | | $eGFR_{cys}$ | | | $GFR_{NMR}$ | | |
|---|---|---|---|---|---|---|---|---|---|
| | Value | CI 2.5% | CI 97.5% | Value | CI 2.5% | CI 97.5% | Value | CI 2.5% | CI 97.5% |
| **n** | 77 | | | 76 | | | 77 | | |
| **RMSE** | 28.4 | | | 34.8 | | | 20.0 | | |
| **Pearson correlation** | 0.82 | 0.73 | 0.88 | 0.61 | 0.45 | 0.74 | 0.85 | 0.78 | 0.90 |
| **P30** | 0.79 | | | 0.67 | | | 0.79 | | |

$$mGFR = GFR_{NMR} + dysfunction$$

| | Df | Sum Sq | Mean Sq | F value | p value |
|---|---|---|---|---|---|
| $GFR_{NMR}$ | 1 | 81312 | 81312 | 197 | <0.0001 |
| dysfunction | 2 | 461 | 230 | 0.56 | 0.57 |
| residuals | 73 | 30135 | 413 | | |

Note: Df indicates degrees of freedom, Sum Sq indicates sum of squares, Mean Sq indicates Mean Squares.

## CONCLUSIONS

**Our results demonstrate that an NMR-based biomarker constellation accurately predicts GFR not only in adults but also in pediatric patients. In fact, this novel method outperformed the established bedside Schwartz equation and the cystatin C-based equation derived from the CKiD cohort. Thus, $GFR_{NMR}$ allows reliable and continuous monitoring of kidney function at the transition from pediatric to adult renal care without the need to switch the estimation equation.**