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Title Utilities for Nephrology

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Description Set of functions to estimate kidney function and other phenotypes of interest in nephrology based on different biomechimal traits.

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nephro-package *Biostatistics utilities for nephrology*

Description

This package contains a set of tools for the estimation of kidney function. Kidney function is assessed by means of the Glomerular Filtration Rate (GFR), which can be estimated using different biomarkers. The most commonly used ones are serum or plasma creatinine and cystatin C.

Included in the package are the following GFR estimating functions: the Modification of Diet in Renal Disease (MDRD) study equations based on four (`MDRD4`) or six (`MDRD6`) parameters (Levey 1999; Levey 2006); the CKD-Epi equations for serum creatinine with the race coefficient (`CKDEpi.creat`) and without the race coefficient (`CKDEpi_RF.creat`); the CKD-Epi equation for cystatin C (`CKDEpi.cys`); the CKD-Epi equation for the combination of creatinine and cystatin C with (`CKDEpi.creat.cys`) and without (`CKDEpi_RF.creat.cys`) the race coefficient (Inker 2012; Inker 2021); the three equations proposed by Stevens 2008 based on cystatin C only (`Stevens.cys1`), age- and sex-weighted cystatin C (`Stevens.cys2`), and a combination of cystatin C and creatinine (`Stevens.creat.cys`); the classic Cockroft and Gault 1976 equation for creatinine clearance estimation (`CG`); the equation by Virga (2007) (`Virga`); the race-free equations developed by the European Kidney Function Consortium (EKFC) including sex and age based on serum creatinine (`EKFC.creat`) (Pottel 2021) and based on serum cystatin C with (`EKFC.cys`) and without (`EKFC_SF.cys`) the sex coefficient (Pottel 2023); the full age spectrum (FAS) equations using serum creatinine (`FAS.creat`) (Pottel 2016), cystatin C (`FAS.cys`), and their combination (`FAS.creat.cys`) (Pottel 2017); the Schwartz bedside formula (`Schwartz.Bedside`) (Schwartz 2009).

A comparative description of several functions included in the initial version of the package can be found in Pattaro (2013). Extensive literature does exist that compares the methods described.

Details

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Author(s)

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References

Citing this package:
- Pattaro C, Riegler P, Stifter G, Modenese M, Minelli C, Pramstaller PP. Estimating the glomerular filtration rate in the general population using different equations: effects on classification and association. *Nephron Clin Pract* 2013; **123**(1-2):102-11.

Formulas:
- Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16**: 31-41.
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- Levey AS, *et al*. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med.* 2006; **145**: 247-54.
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- Pottel H, *et al*. Estimating glomerular filtration rate for the full age spectrum from serum creatinine and cystatin C *Nephrol Dial Transplant* 2017; **32**: 497-507.
- Schwartz GJ, *et al*. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 2009; **20**:629-637.

On IDMS calibration:
- Levey AS, *et al*. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem* 2007; **53**:766-72.
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- Skali H, *et al*. Prognostic assessment of estimated glomerular filtration rate by the new Chronic

Kidney Disease Epidemiology Collaboration equation in comparison with the Modification of Diet in Renal Disease Study equation. *Am Heart J* 2011; **162**:548-54.

Examples

```
# Comparison between different equations

creat <- c(0.8, 0.9, 1.0, 1.1, 1.2, 1.3)
cyst  <- c(1.1, 0.95, 1.1, 1.0, 1.3, 1.2)
sex <- c(1, 1, 1, 0, 0, 0)
age <- c(60, 65, 43, 82, 71, 55)
ethn <- round(runif(6))
wt <- c(70, 80, 60, 55, 87, 71)

eGFR <- data.frame(creat, cyst)
eGFR$MDRD4 <- MDRD4(creat, sex, age, ethn, 'IDMS')
eGFR$CKDEpi.creat <- CKDEpi.creat(creat, sex, age, ethn)
eGFR$CKDEpi_RF.creat <- CKDEpi_RF.creat(creat, sex, age)
eGFR$CKDEpi.cys <- CKDEpi.cys(cyst, sex, age)
eGFR$CKDEpi.creat.cys <- CKDEpi.creat.cys(creat, cyst, sex, age, ethn)
eGFR$CKDEpi_RF.creat.cys <- CKDEpi_RF.creat.cys(creat, cyst, sex, age)
eGFR$Stevens.cys1 <- Stevens.cys1(cyst)
eGFR$Stevens.cys2 <- Stevens.cys2(cyst, sex, age, ethn)
eGFR$Stevens.creat.cys <- Stevens.creat.cys(creat, cyst, sex, age, ethn)
eGFR$cg <- CG(creat, sex, age, wt)
eGFR$virga <- Virga(creat, sex, age, wt)

pairs(eGFR[,3:13])

# For use with non-IDMS calibrated creatinine
# several authors (see references) suggested
# a 5% creatinine adjustment

creat <- c(0.8, 0.9, 1.0, 1.1, 1.2, 1.3)
sex <- c(1, 1, 1, 0, 0, 0)
age <- c(60, 65, 43, 82, 71, 55)
ethn <- round(runif(6))
gfr <- CKDEpi.creat(0.95*creat, sex, age, ethn)
```

CG *Cockroft and Gault equation*

Description

Creatinine clearance is estimated with the Cockroft and Gault formula.

Usage

```
CG(creatinine, sex, age, wt)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years
wt	Numeric vector with weight in kg

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16**: 31-41.

See Also

CKDEpi.creat, MDRD4, Virga

CKDEpi.creat *CKD-EPI equation for serum creatinine*

Description

GFR is estimated with the CKD-EPI Study equation based on IDMS serum or plasma creatinine.

Usage

```
CKDEpi.creat(creatinine, sex, age, ethnicity)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years
ethnicity	Numeric vector with 0 for non-Black and 1 for Black individuals

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Inker LA, *et al*. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012; **367**: 20-29.

See Also

`CKDEpi.creat.cys`, `CKDEpi.cys`, `CKDEpi_RF.creat`

`CKDEpi.creat.cys` *CKD-EPI equation for creatinine and cystatin C*

Description

CKD-EPI equation to estimate GFR based on a combination of creatinine and cystatin C

Usage

```
CKDEpi.creat.cys(creatinine, cystatin, sex, age, ethnicity)
```

Arguments

`creatinine`	Numeric vector with serum or plasma creatinine values in mg/dl
`cystatin`	Numeric vector with serum or plasma cystatin C values in mg/dl
`sex`	Numeric vector with 0 for females and 1 for males
`age`	Numeric vector with age in years
`ethnicity`	Numeric vector with 0 for non-Black and 1 for Black individuals

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Inker LA, *et al*. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012; **367**: 20-29.

See Also

`CKDEpi.creat`, `CKDEpi.cys`, `CKDEpi_RF.creat.cys`

CKDEpi.cys *CKD-EPI equation for cystatin C*

Description

GFR is estimated with the CKD-EPI equation for cystatin C proposed by Inker et al., N Engl J Med 2012

Usage

```
CKDEpi.cys(cystatin, sex, age)
```

Arguments

cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Inker LA, *et al*. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012; **367**: 20-29.

See Also

CKDEpi.creat, CKDEpi.creat.cys

CKDEpi_RF.creat *Race-free CKD-EPI equation for serum creatinine*

Description

GFR is estimated with the CKD-EPI Study equation based on serum creatinine without the ethnicity coefficient.

Usage

```
CKDEpi_RF.creat(creatinine, sex, age)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Ryosuke Fujii

References

Inker LA, *et al*. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med* 2021; **385**: 1737-1749.

See Also

CKDEpi.creat, CKDEpi.creat.cys, CKDEpi.cys, CKDEpi_RF.creat.cys

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CKDEpi_RF.creat.cys *Race-free CKD-EPI equation for serum creatinine and cystatin C*

Description

CKD-EPI equation to estimate GFR based on a combination of creatinine and cystatin C without the ethnicity coefficient

Usage

```
CKDEpi_RF.creat.cys(creatinine, cystatin, sex, age)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Ryosuke Fujii

References

Inker LA, *et al*. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med* 2021; **385**: 1737-1749.

See Also

`CKDEpi.creat`, `CKDEpi.creat.cys`, `CKDEpi.cys`, `CKDEpi_RF.creat`

`EKFC.creat` *EKFC equation for serum creatinine*

Description

EKFC equation for serum creatinine modified from FAS equation

Usage

```
EKFC.creat(creatinine, sex, age)
```

Arguments

`creatinine`	Numeric vector with serum or plasma creatinine values in mg/dl
`sex`	Numeric vector with 0 for females and 1 for males
`age`	Numeric vector with age in years

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H, *et al*. Development and Validation of a Modified Full Age Spectrum Creatinine-Based Equation to Estimate Glomerular Filtration Rate : A Cross-sectional Analysis of Pooled Data. *N Engl J Med* 2021; **174**: 183-191.

See Also

`EKFC.cys`, `CKDEpi.creat`

EKFC.cys *EKFC equation for cystatin C*

Description

EKFC equation for cystatin C that includes the sex coefficient, as proposed by Pottel et al., *N Engl J Med* 2023

Usage

```
EKFC.cys(cystatin, sex, age)
```

Arguments

cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H, *et al*. Cystatin C-Based Equation to Estimate GFR without the Inclusion of Race and Sex. *N Engl J Med* 2023; **388**: 333-343.

See Also

EKFC_SF.cys

EKFC_SF.cys *Sex-free EKFC equation for cystatin C*

Description

EKFC equation for cystatin C without the sex coefficient as proposed by Pottel et al., *N Engl J Med* 2023

Usage

```
EKFC_SF.cys(cystatin, age)
```

Arguments

cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
age	Numeric vector with age in years

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H, *et al*. Cystatin C-Based Equation to Estimate GFR without the Inclusion of Race and Sex. *N Engl J Med* 2023; **388**: 333-343.

See Also

EKFC.cys

FAS.creat *FAS equation for serum creatinine*

Description

Full age spectrum (FAS) equation to estimate GFR based on serum creatinine

Usage

```
FAS.creat(creatinine, sex, age)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H., *et al*. An estimated glomerular filtration rate equation for the full age spectrum. *Nephrol Dial Transplant.* 2016; **5**: 798-806.

See Also

FAS.creat.cys, FAS.cys

FAS.creat.cys *FAS equation for creatinine and cystatin C*

Description

Full age spectrum (FAS) GFR estimation based on serum creatinine and cystatin C

Usage

```
FAS.creat.cys(creatinine, cystatin, sex,age)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H., *et al*. An estimated glomerular filtration rate equation for the full age spectrum from serum creatinine and cystatin C. *Nephrol Dial Transplant.* 2017; **32**: 497-507.

See Also

FAS.cys

FAS.cys *FAS equation for cystatin C*

Description

Full age spectrum (FAS) GFR estimation based on cystatin C

Usage

```
FAS.cys(cystatin, sex, age)
```

Arguments

cystatin	Numeric vector with serum or plasma cystatin values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Janina Herold

References

Pottel, H., *et al*. An estimated glomerular filtration rate equation for the full age spectrum from serum creatinine and cystatin C. *Nephrol Dial Transplant.* 2017; **32**: 497-507.

See Also

FAS.creat, FAS.creat.cys

MDRD4 *Four-parameter MDRD study equation*

Description

GFR is estimated with the 4-parameter Modification of Diet in Renal Disease (MDRD) study equation.

Usage

```
MDRD4(creatinine, sex, age, ethnicity, method = "IDMS")
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years
ethnicity	Numeric vector with 0 for non-Black and 1 for Black individuals
method	Defaults is 'IDMS' for IDMS-traceable creatinine; write 'other' if not IDMS

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Levey AS, *et al*. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999; **130**(6): 461-70.
Levey AS, *et al*. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med.* 2006; **145**: 247-254.

See Also

CKDEpi.creat, MDRD6, CG

MDRD6 *Six-parameter MDRD study equation*

Description

GFR is estimated with the 6-parameter Modification of Diet in Renal Disease (MDRD) study equation.

Usage

```
MDRD6(creatinine, sex, age, albumin, BUN, ethnicity, method = 'IDMS')
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years
albumin	Numeric vector with serum or plasma albumin in g/dl
BUN	Numeric vector with blood urea nitrogen levels in mg/dl
ethnicity	Numeric vector with 0 for non-Black and 1 for Black individuals
method	Defaults is 'IDMS' for IDMS-traceable creatinine; write 'other' if not IDMS

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Levey AS, *et al*. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999; **130**(6): 461-70.
Levey AS, *et al*. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006; **145**: 247-254.

See Also

MDRD4

Schwartz.Bedside *Bedside IDMS-traceable Schwartz GFR Calculator for Children*

Description

GFR is estimated with the Bedside Schwartz equation for Children based on IDMS serum or plasma creatinine.
This equation is valid in the 1-17 years age range.

Usage

```
Schwartz.Bedside(creatinine, ht, age)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
ht	Numeric vector with height in cm
age	Numeric vector with age in years

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Andrew Srisuwananukorn

References

Schwartz GJ, *et al*. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol* 2009; **20**: 629-637.

Stevens.creat.cys *Stevens' formula for a combination of serum creatinine and cystatin C*

Description

GFR estimation using the 3rd formula proposed by Stevens et al. (Am J Kidney Dis 2008), which combines creatinine and cystatin C

Usage

```
Stevens.creat.cys(creatinine, cystatin, sex, age, ethnicity)
```

Arguments

creatinine	Numeric vector with serum or plasma creatinine values in mg/dl
cystatin	Numeric vector with serum or plasma cystatin C values in mg/l
sex	Numeric vector with 0 for females and 1 for males
age	Numeric vector with age in years
ethnicity	Numeric vector with 0 for non-Black and 1 for Black individuals

Value

The function returns a numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Stevens LA, *et al*. Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. *Am J Kidney Dis* 2008; **51**: 395-406.

See Also

`CKDEpi.creat.cys`

`Stevens.cys1` *GFR estimation using serum cystatin C*

Description

GFR is estimated with the 1st formula proposed by Stevens et al. (Am J Kidney Dis 2008), i.e.: as a simple transformation of cystatin C, without using any other information

Usage

```
Stevens.cys1(cystatin)
```

Arguments

`cystatin`	Numeric vector with serum or plasma cystatin C values in mg/l

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Stevens LA, *et al*. Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. *Am J Kidney Dis* 2008; **51**: 395-406.

See Also

`Stevens.cys2`, `Stevens.creat.cys`, `CKDEpi.cys`

`Stevens.cys2` *Stevens' formula for serum cystatin C, age, and sex*

Description

GFR is estimated with the 2nd formula proposed by Stevens et al. (Am J Kidney Dis 2008), where cystatin C is weighted by sex and age

Usage

```
Stevens.cys2(cystatin, sex, age, ethnicity)
```

Arguments

`cystatin`	Numeric vector with serum or plasma cystatin C values in mg/l
`sex`	Numeric vector with 0 for females and 1 for males
`age`	Numeric vector with age in years
`ethnicity`	Numeric vector with 0 for non-Black and 1 for Black individuals

Value

A numeric vector with eGFR values in ml/min/1.73 m^2.

Author(s)

Cristian Pattaro

References

Stevens LA, *et al*. Estimating GFR using serum cystatin C alone and in combination with serum creatinine: a pooled analysis of 3,418 individuals with CKD. *Am J Kidney Dis* 2008; **51**: 395-406.

See Also

`Stevens.cys1`, `Stevens.creat.cys`, `CKDEpi.cys`

`Virga` *Virga's formula*

Description

Virga's formula is based on serum creatinine, sex, age, and body weight.

Usage

```
Virga(creatinine, sex, age, wt)
```

Arguments

`creatinine`	Numeric vector with serum or plasma creatinine values in mg/dl
`sex`	Numeric 0/1 vector: 0 for females, 1 for males
`age`	Numeric vector with age in years
`wt`	Numeric vector with weight in kg

Value

A numeric vector with eGFR values in *ml/min/1.73 m^2*

Author(s)

Cristian Pattaro

References

Virga G, *et al*. A new equation for estimating renal function using age, body weight and serum creatinine. *Nephron Clin Pract* 2007; **105**: c43-53.

See Also

`CG`, `MDRD4`

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