User manual
for the
CKD-EPI eGFRcr calculator

Version 3, June 2026, in English

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1. The Evidencio platform

The Evidencio platform facilitates the creation, use, validation and implementation of medical prediction models and clinical decision support tools. This User Manual specifically relates to the CKD-EPI eGFRcr equation, (which covers the eGFR 2009 CKD-EPI creatinine equation, the eGFR 2009 CKD-EPI creatinine equation (without race), and the eGFR 2021 CKD-EPI creatinine equation. The User Manual can also be referred to as the Instructions for Use (IFU). The CKD-EPI eGFRcr calculator meets the requirements laid down in: Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. Compliance with the applicable regulations is provided by means of declaration of conformity.

Throughout this manual CE-marked content and the term medical device are used interchangeably.

2. Disclaimer

Evidencio provides certain CE-marked information, calculators, equations, and algorithms (tools) on any of its websites, applications, apps, or services. These tools may only be used in accordance with the intended use / intended purpose that has been published with the respective CE-marked tool.

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The CE-marked content on the platform is to be regarded as a specific set of tools, apart from the general platform content. Any available content, on any of the websites, applications, apps, or services provided by Evidencio that is not clearly labelled as a CE-marked tool is explicitly not covered by this disclaimer for CE-marked content, the general Evidencio Disclaimer for non-CE-marked content applies.
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Your use of the websites, applications, apps, or services provided by Evidencio is subject to our Terms & Conditions, which can be found here: https://www.evidencio.com/terms-conditions.

⚠ 3. Warnings for CE-marked content

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer on: https://www.evidencio.com/disclaimer. This tool is only to be used by healthcare professionals, and is not for patient use.

Always read the intended use before using this tool.

Always make sure the patient complies with the clinical indications and clinical contra-indications as stated on the Evidencio website, and in **paragraphs 6.3.1** and **6.3.2** of this user manual respectively.

Before reading the result, double check the filled in values to prevent errors.

Results that concern risk percentages, do not guarantee certain outcomes. When there is a risk present, do not expect an event to not occur at all, even if the risk is very small. Conversely, a high risk does not guarantee that an event will occur.

This algorithm is only intended for use in settings where the usage and result of an algorithm are never immediately needed.

The data used to perform the calculations is stored by Evidencio to enhance algorithm function and allow issues to be traceable for further improvements. For details, see the privacy policy on our website at: https://www.evidencio.com/privacy-policy.

3.1. Notice to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the country in which you, the reader, are established. A competent authority is the institute that governs all issues related to medical devices in a country.

Please contact Evidencio when you suspect any malfunction or changes in the performance of a medical device. Do not use the device, until Evidencio replies to your message that it is safe to start using it again.

4. Device description CKD-EPI eGFRcr calculator

The CKD-EPI eGFRcr calculator is intended to be used by professional users who are capable of operating the device and interpreting its results. It can be used to estimate the Glomerular Filtration Rate in patients to assess kidney functioning.

The CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equations were developed in an effort to create a more precise formula to estimate glomerular filtrate rate (GFR) from serum creatinine, age, sex, and originally race. Especially when actual GFR is >60 mL/min per 1.73m^2. The CKD-EPI released their original equations in 2009, which included race as a variable. In 2021, they used the same data to derive a new equation that does not include race as an explanatory variable. The CKD-EPI eGFRcr is intended for adults without Acute Kidney injury, consult the intended purpose or user manual for a more extensive description. The CKD-EPI eGFRcr calculators are generally considered to be the state of the art, but which version is recommended differs geographically.

The CKD-EPI eGFRcr calculator is a collective name used here to refer to three related medical devices which can be used independently; the eGFR 2009 CKD-EPI creatinine equation, the eGFR 2009 CKD-EPI creatinine equation (without race) and the eGFR 2021 CKD-EPI creatinine equation. This singular term is used for clarity and brevity when something applies to all 3 models. Differences between the separate devices will be mentioned when applicable.

The MDSW's underlying mathematical formula is based on a least-squares linear regression with nonparametric smoothing splines and linear splines for observed nonlinearity.

The calculation of the algorithm is performed by communication with the Evidencio platform, hosted at www.evidencio.com. The algorithm is also accessible by 3rd party applications through the API and iFrame implementation. The Evidencio platform is managed under Evidencio's certified quality management system that ensures the correctness of calculations and availability of its services.

The Summary of Safety and Performance for this device will be made available via EUDAMED once the relevant module is fully operational. In the meantime, the Summary of Safety and Performance can be requested from the manufacturer and will be provided without undue delay.

4.1. Lifetime, residual risks and side effects

The CKD-EPI eGFRcr calculator is software, and does not expire. The lifetime is initially set at 5 years from certification, if the state of the art does not change in such a way as to negatively affect the benefit-risk of the device, the lifetime can be extended.

No steps are required to be undertaken by the user to decommission a product when it is taken off the market. If the lifetime is not extended, a notice will be placed on the algorithm page on the platform. When a device is taken off the market, users may be informed about this (e.g. through e-mail).

Evidencio has identified a series of risks associated with the use of this algorithm.

The CKD-EPI eGFRcr calculator is a low and medium-risk device, there are no noticeable risks involved outside of possible mis-estimation of eGFR, and all residual risks are accepted.

Most risks can be defined into two main groups, depending on their outcome.

a) The risk calculation was wrong or;
b) The MDSW prediction algorithm is inaccessible.

A wrong risk calculation can be the result of erroneous input values or an error in the mathematical calculation. Technical risks, including the erroneous calculations or the inaccessibility due to a technical error, have been mitigated when possible. These measures focussed on reducing the risks' probability and severity. Concluding that the risks could not be mitigated

further, the residual risks were classified as *low and medium-level and acceptable.* The CKD-EPI eGFRcr calculator does not have any direct side effects.

5. Electronic label

The electronic label of this device contains the following information:

CE 2797	**Name of the device**	CKD-EPI eGFRcr calculator
	Manufacturer information	Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
LOT	**LOT number** eGFR 2009 CKD-EPI creatinine equation: eGFR 2009 CKD-EPI creatinine equation (without race): eGFR 2021 CKD-EPI creatinine equation:	 V-1.26-9984.26.06.29 V-2.1-9984.26.06.29 V-3.1-9984.26.06.29
UDI	**UDI number** eGFR 2009 CKD-EPI creatinine equation: eGFR 2009 CKD-EPI creatinine equation (without race): eGFR 2021 CKD-EPI creatinine equation:	 (01)08720938015243(8012)v1.26(4326)260629(240)9984 (01)08720938015250(8012)v2.1(4326)260629(240)9984 (01)08720938015267(8012)v3.1(4326)260629(240)9984
IVD	**IVD indication**	*In vitro* diagnostic medical device

The electronic label can be found on the Evidencio website, see also section **I** and **Figure 8** in **Chapter 10**.

The electronic label on the website further contains the option to download the **User Manual** and **Declaration of conformity** (DoC).

5.1. LOT number

The LOT number indicates the algorithm version, the algorithm identifier, and the algorithm publication date. Publication date is indicated as YY.MM.DD.

5.2. UDI number

Stands for Unique Device Identifier (UDI) number, which is an international tool that helps users identify and find information on products. Evidencio's UDI's have the following format:

(01)[UDI-DI number](8012)[versionnumber](4326)[releasedate](240)[identificationnumber]

The UDI-DI (Device Identifier) number is a unique numeric code. For each medical device of Evidencio, a unique UDI-DI is ascribed. This UDI-DI is used as an "access key" for information stored in a unique device identification database (UDID). Information on Evidencio's medical devices can be found by searching for the UDI-DI number in the following data base: https://gepir.gs1.org/index.php/search-by-gtin.

The version number, also part of the UDI, is linked to one of the 3 device sub-models. Version 1.x for eGFR 2009 CKD-EPI creatinine equation, Version 2.x for eGFR 2009 CKD-EPI creatinine equation (without race), and Version 3.x for eGFR 2021 CKD-EPI creatinine equation.

6. Intended purpose

6.1. Intended use

The CKD-EPI eGFRcr calculator is intended to be used by professional users who are capable of operating the device and interpreting its results. It can be used to estimate the Glomerular Filtration Rate in patients to assess kidney functioning.

The CKD-EPI eGFRcr calculator consists of three different equations that largely overlap in required input variables and presented outcome.

The device combines Age, Sex, and Serum Creatinine (and Race for the eGFR 2009 CKD-EPI creatinine equation) to estimate Glomerular Filtration rate. Serum Creatinine requires a blood sample from the patient.

The device is intended to be used for patients where the Glomerular Filtration Rate should be estimated. The result of the CKD-EPI eGFRcr calculator is intended to be reviewed and interpreted by healthcare professionals only. The device is not intended for use by patients on their own.

The CKD-EPI eGFRcr calculator is medical device software that automates the calculation of the formula(s). It requires quantitative and qualitative inputs to provide a quantitative output.

The CKD-EPI eGFRcr calculator is not intended to replace clinical decision-making, it can only provide an estimation of the patient's GFR to the user based on the serum creatinine measurement and clinical features. The user can use this information to support clinical decision-making regarding potential kidney dysfunction, which is relevant in a wide variety of situations.

6.2. Clinical benefit

The CKD-EPI eGFRcr calculator is intended to assist healthcare professionals with patients that have relevant and specified clinical outcome parameters. Concretely, this is achieved by estimating the GFR as a measure of kidney functioning, to support clinical decision-making where kidney function plays a role. Correct functioning of the CKD-EPI eGFRcr calculator can result in the following clinical benefit:

- Use of the CKD-EPI eGFRcr calculator allows for the estimation of the Glomerular Filtration Rate.

6.3. Intended target population and exclusion

The CKD-EPI eGFRcr calculator is intended to be used only for a specific group of patients, corresponding to the below indications and contra-indications.

6.3.1. Clinical indication

The CKD-EPI eGFRcr calculator should be used for patients who meet the following inclusion criteria:

- 18 years or older

6.3.2. Clinical contra-indications

The CKD-EPI eGFRcr calculator should not be used for patients who meet one or more of the following exclusion criteria:

- Patients with Acute Kidney Injury
- Patients where Creatinine measurements were not taken with a valid calibration traceable to international standard reference material, and with minimal bias when compared to IDSM reference methodology.

The CKD-EPI eGFRcr calculator and other Creatinine based GFR estimation equations are known to sometimes perform inadequately in the following clinical populations/with the following features. Care should be taken, especially if the results do not meet expectations:

- Body composition:
  - Amputation,
  - Body Building
  - Reduced Lean Body Mass
- Diet:

- High Protein or creatine supplements
- Cooked meat consumption
- Vegetarianism

- Muscle Wasting
  - Muscle wasting disease
  - Heavy Physical exercise (e.g. Marathon Running)
  - Chronic Severe Illness
- Clinical conditions:
  - Pregnancy
  - Cystic fibrosis/Cirrhosis
  - Anorexia Nervosa
  - Edematous state
  - Diabetes
    - Hyperfiltration
- Certain Medications influencing tubular secretion, or nephrotoxic drugs with a narrow window, for example:
  - Cimetidine, Trimethoprim, Fenofibrate, Dolutegravir, Tyrosine kinase inhibitors and Certain Antibiotics
- Other:
  - EGFR values exceeding anticipated values or normal physiological range
  - Very low GFR

6.4. User profile

The result of the CKD-EPI eGFRcr calculator is intended to be reviewed and interpreted by healthcare professionals. Results shall always be reviewed and interpreted by healthcare professionals, in the context of the patient's clinical history and other diagnostic test results. Healthcare professionals do not require additional training prior to the use of the medical device. The device is not intended for use by patients on their own.

6.5. Intended use environment

The MDSW can be used as made available on the Evidencio platform in any actively supported web-browser on personal computers, mobile devices, or tablet PCs. Users can manually enter the required input data through the user interface. In addition, the MDSW is available as an embedded view via Evidencio's iFrame representation. Automated calculation of the device is enabled through Evidencio's API. The device is only intended for use in healthcare settings where the immediate application and outcomes of the device are not required. The device is not intended to be used at the bedside of the patient.

6.6. Physical interaction

The MDSW is stand-alone software and does not come into contact with any bodily or other material of the patient, user or otherwise.

6.7. History/ versions of the MDSW

The original version of the CKD-EPI eGFRcr calculator was developed in 2009 by Levey et al. In 2021, Inker et al. created a new version that did not include Race as an explanatory variable in the derivation. The 2021 version, as well as the 2009 version, and a modified 2009 version with race removed as a factor, are concerned in this document, and together are called the CKD-EPI eGFRcr calculator.

eGFR 2009 CKD-EPI creatinine equation	(Version 1.XX)
eGFR 2009 CKD-EPI creatinine equation (without race)	(Version 2.XX)
eGFR 2021 CKD-EPI creatinine equation	(Version 3.XX)

6.8. Functioning physical principle

The CKD-EPI eGFRcr calculator's underlying model concerns a custom mathematical equation. The acquisition and processing of the data, the analyses to assemble the relevant criteria for the CKD-EPI eGFRcr calculator as well as the setup and refinement of the CKD-EPI eGFRcr calculator are described in the original study/studies from Inker et al. and Levey et al. Entering the details of an individual in the MDSW initiates the calculation of the eGFR of the patient.

7. Additional information

7.1. Details

Algorithm author	Evidencio	
Root algorithm ID	9984	
	Version number	**Revision date**
eGFR 2009 CKD-EPI creatinine equation	1.26	29 JUN 2026
eGFR 2009 CKD-EPI creatinine equation (without race)	2.1	29 JUN 2026
eGFR 2021 CKD-EPI creatinine equation	3.1	29 JUN 2026
Speciality	Nephrology	
Model type	Custom calculation	
MeSH terms	• Kidney • Creatinine • Glomerular Filtration Rate	

7.2. Input variables

To perform the calculations successfully, the devices comprising the CKD-EPI eGFRcr calculator require the input of all input variables. Which input variables are part of the equation differs between the devices, with the race variable applying only to the eGFR 2009 CKD-EPI creatinine equation, V1.x. An overview is provided in **Table 1** below.

Table 1. Variables used as input for the CKD-EPI eGFRcr calculator.

Name	Description	Type	Range (step size)	Units
Age	The age of the patient	Continuous	18-100 (1)	*Year*
Sex	The sex of the patient	Categorical	Male/Female	*N/A*
Race	The race of the patient For use in 2009 CKD-EPI eGFRcr (ASR) equation only. Consider using the 2009 CKD-EPI eGFRcr (ASR-NB) version without race.	Categorical	Black/Non-Black	*N/A*
Serum Creatinine	Serum Creatinine level	Continuous	0.1-25 (0.1)	*mg/dL*
			10-1000 (1)	*µmol/L*

7.3. Equations

The CKD-EPI eGFRcr calculator uses the following equations in order to estimate the Glomerular Filtration Rate. The min() and the max() functions used within the equation, select the minimum, and the maximum values, respectively between the *serum Creatinine / (0.9 or 0.7)*, and 1. This is also described by *Levey et al*. in the derivation paper of the equations.

Condition	Formula
Sex=Male	$141 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-0.411} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-1.209} \cdot 0.9929^{\text{Age}} \cdot \text{Race}$
Sex=Female	$141 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-0.329} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-1.209} \cdot 0.9929^{\text{Age}} \cdot 1.018 \cdot \text{Race}$

Figure 3. The Conditions and Formula of the eGFR 2009 CKD-EPI creatinine equation.

Condition	Formula
Sex=Male	$141 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-0.411} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-1.209} \cdot 0.9929^{\text{Age}}$
Sex=Female	$141 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-0.329} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-1.209} \cdot 0.9929^{\text{Age}} \cdot 1.018$

Figure 2. The Conditions and Formula of the eGFR 2009 CKD-EPI creatinine equation (without race).

Condition	Formula
Sex=Male	$142 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-0.302} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.9}, 1\right)^{-1.200} \cdot 0.9938^{\text{Age}}$
Sex=Female	$142 \cdot \min\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-0.241} \cdot \max\left(\frac{\text{Serum Creatinine}}{0.7}, 1\right)^{-1.200} \cdot 0.9938^{\text{Age}} \cdot 1.012$

Figure 1. The Conditions and Formula of the eGFR 2021 CKD-EPI creatinine equation.

7.4. Result interpretation

Primary outcome

The primary output of this device is given as estimated Glomerular Filtration Rate in ml/min/1.73m^2, which is abbreviated as eGFR. The eGFR is estimated through serum Creatinine concentrations. Generally, healthy GFR values lie between 90 and 120 ml/min/1.73m^2. A GFR between 60 and 90 may point to early-stage kidney disease. A GFR between 15 and 60 is indicative of kidney disease a GFR below 15 is a sign of kidney failure. eGFRcr helps provide an estimate, but does not always reflect the actual GFR.

One of the disadvantages of the CKD-EPI is that it only accounts for Age and Sex (and Race, in the 2009 equations) without taking into account body shape. As Creatinine is produced by muscle tissue, production levels differ between different patients, as people of the same age and gender may have drastically different amounts of muscle tissue, which influences eGFR calculation.

Conditional information

The following table shows the conditional descriptions for the CKD-EPI eGFRcr calculator, matching estimated eGFRcr to the associated KDIGO GFR category.

Table 2. Conditional information shown for the CKD-EPI eGFRcr calculator.

Condition	Description
90ml/min/1.73m^2 ≤ eGFRcr	GFR equal to or above 90ml/min/1.73m^2 corresponds to the following KDIGO GFR category: G1: Normal or High
60ml/min/1.73m^2 ≤ eGFRcr < 90ml/min/1.73m^2	GFR between 60 and 90ml/min/1.73m^2 corresponds to the following KDIGO GFR category: G2: Mildly Decreased
45ml/min/1.73m^2 ≤ eGFRcr < 60ml/min/1.73m^2	GFR between 45 and 60ml/min/1.73m2 corresponds to the following KDIGO GFR category: G3a: Mildly to Moderately Decreased
30ml/min/1.73m^2 ≤ eGFRcr < 45ml/min/1.73m^2	GFR between 30 and 45ml/min/1.73m^2 corresponds to the following KDIGO GFR category: G3b: Moderately to Severely Decreased
15ml/min/1.73m^2 ≤ eGFRcr < 30ml/min/1.73m^2	GFR between 15 and 30ml/min/1.73m^2 corresponds to the following KDIGO GFR category: G4: Severely Decreased
eGFRcr < 15ml/min/1.73m^2	GFR below 15ml/min/1.73m^2 corresponds to the following KDIGO GFR category: G5: Kidney Failure

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7.5. Study characteristics

The CKD-EPI eGFRcr calculators were developed in an effort to create a more precise formula to estimate glomerular filtrate rate (GFR) from serum creatinine and other readily available clinical parameters, especially at when actual GFR is >60 mL/min per 1.73m2. The original equations were derived in 2009 and included Race as an explanatory variable in model derivation. In 2021, the CKD-EPI derived a new set of equations using the same data-set, without using Race as a variable. Evidencio's version of the CKD-EPI eGFRcr calculators includes three versions of the equations.

The original 2009 equations derived using race as an explanatory variable in addition to Age, Sex and serum Creatinine. (**eGFR 2009 CKD-EPI creatinine equation**)

The 2009 equations, derived using Race, Age, Sex and serum Creatinine as explanatory variables, without including the race variable in the calculation. (**eGFR 2009 CKD-EPI creatinine equation (without race)**)

The 2021 equations, derived without using race as an explanatory variable, using only Age and Sex in addition to serum Creatinine as explanatory variables. (**eGFR 2021 CKD-EPI creatinine equation**)

New eGFR equations that incorporate creatinine and cystatin C but omit race are more accurate and led to smaller differences between Black participants and non-Black participants than new equations without race with either creatinine or cystatin C alone.

Information on the characteristics of the patient data used to derive and validate the algorithm is provided in table **Table 3** and **Table 4**.

Table 3. Patient characteristics on the derivation cohort.

NAME	MEAN	SD	UNIT
Age	47	14.8	Year
BMI	28.2	6.1	kg/m^2
Measured GFR	67.6	39.6	mL/min/1.73 m^2
Creatinine	1.66	1.16	mg/dL

Table 4. Categorical patient characteristics on the derivation cohort.

NAME	SUBSET / GROUP	NR. OF PATIENTS (%)
Age	<40yr	2921 (35%)
	40-65 yr	4309 (52%)
	>65 yr	1024 (12%)
BMI	<20	285 (3%)
	20 to <25	2446 (30%)
	25 to <30	2923 (35%)
	≥30	2600 (31%)
Diabetes (data available for 3616 patients)	Yes	2406 (67%)
Kidney-donor candidate	Yes	1030 (12%)
Measured GFR Category	<30 mL/min/1.73 m^2	1722 (21%)
	30 to <60 mL/min/1.73 m^2	2334 (28%)
	60 to <90 mL/min/1.73 m^2	1669 (20%)
	≥90 mL/min/1.73 m^2	2529 (31%)

7.6. Supporting publication & Related files

Several relevant studies, such as the original derivation study by Levey et al. are contained in **Table 5**. These publications have tags to identify their link with the model. Examples of relevant tags are; “Peer review”, “Internal validation”, “External validation”, and “TRIPOD”. Publications that have the tags: “Internal validation” or “External validation”, contain data on the performance characteristics of the device.

Table 5. Overview of selection of supporting publications & Related files.

Development Paper of the original 2009 equations ***External validation*** ***Internal validation***	**A New Equation to Estimate Glomerular Filtration Rate** *Andrew S. Levey, MD; Lesley A. Stevens, MD, MS; Christopher H. Schmid, PhD; Yaping (Lucy) Zhang, MS; Alejandro F. Castro III, MPH; Harold I. Feldman, MD, MSCE; John W. Kusek, PhD; Paul Eggers, PhD; Frederick Van Lente, PhD; Tom Greene, PhD; and Josef Coresh, MD, PhD, MHS, for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration)* *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2763564/* DOI: 10.7326/0003-4819-150-9-200905050-00006
Development Paper of the 2021equation, including comparison to 2009 equations in a US population. ***External validation*** ***Model updating*** ***Internal validation***	**New Creatinine- and Cystatin C–Based Equations to Estimate GFR without Race** *L.A. Inker, N.D. Eneanya, J. Coresh, H. Tighiouart, D. Wang, Y. Sang, D.C. Crews, A. Doria, M.M. Estrella, M. Froissart, M.E. Grams, T. Greene, A. Grubb, V. Gudnason, O.M. Gutiérrez, R. Kalil, A.B. Karger, M. Mauer, G. Navis, R.G. Nelson, E.D. Poggio, R. Rodby, P. Rossing, A.D. Rule, E. Selvin, J.C. Seegmiller, M.G. Shlipak, V.E. Torres, W. Yang, S.H. Ballew, S.J. Couture, N.R. Powe, and A.S. Levey, for the Chronic Kidney Disease Epidemiology Collaboration* *https://www.nejm.org/doi/full/10.1056/NEJMoa2102953* DOI: 10.1056/NEJMoa2102953

Document discussing the different CKD-EPI equations and their performance in a European cohort. ***Information on topic***	**Removing race from the CKD-EPI equation and its impact on prognosis in a predominantly White European population** *Edouard L Fu, Josef Coresh, Morgan E Grams, Catherine M Clase, Carl-Gustaf Elinder, Julie Paik, Chava L Ramspek, Lesley A Inker, Andrew S Levey, Friedo W Dekker, Juan J Carrero* *https://academic.oup.com/ndt/article/38/1/119/6605926* https://doi.org/10.1093/ndt/gfac197

7.7. Analytical performance characteristics

To demonstrate the analytical performance of the CKD-EPI eGFRcr calculator, evidence was collected based on four requirements. This led to the following results:

- A code review and functional test showed that the calculation of the online tool provides the exact same results as described in the papers by Levey et al. (2009) and Inker et al. (2021).
- Monthly uptime reports show that the device is available online with an uptime of at least 99%.
- The calculation time is within 2 minutes, otherwise an error is given to the manufacturer, this is analysed each 6 months in the analysis of quality data.
- Absence of unacceptable cybersecurity vulnerabilities.

7.8. Clinical performance characteristics

The CKD-EPI eGFRcr calculator is accurate, with P_{30} (percentage of estimations within 30% of measured value) values generally above 80%, and a median bias of less than 10 ml/min/1.73m^2. The results of Inker et al (2021) are shown below. Different studies provided similar performance levels, with some variation between populations and equations used.

Table 6. Performance characteristics of the CKD-EPI eGFRcr calculator's different equations in the original 2021 study by Inker et al.

Equation	Accuracy (P_{30}) (95% CI)	Bias (ml/min/1.73 m^2) (95% CI)
eGFR 2009 CKD-EPI creatinine equation	Black: 85.1 (82.2 to 87.9) Non-Black: 89.5 (88.5 to 90.4)	Black: −3.7 (−5.4 to −1.8) Non-Black: −0.5 (−0.9 to 0.0)
eGFR 2009 CKD-EPI creatinine equation (without race)	Black: 86.4 (83.4 to 89.1) Non-Black: 89.5 (88.5 to 90.4)	Black: 7.1 (5.9 to 8.8) Non-Black: −0.5 (−0.9 to 0.0)
eGFR 2021 CKD-EPI creatinine equation	Black: 87.2 (84.5 to 90.0) Non-Black: 86.5 (85.4 to 87.6)	Black: 3.6 (1.8 to 5.5) Non-Black: −3.9 (−4.4 to −3.4)

7.9. Release notes

The release notes for each publicly available version of the device can be found on the Evidencio website page for the CKD-EPI eGFRcr calculator: https://www.evidencio.com/models/show/9984, selecting the correct device and, when applicable, device version, and clicking on Release Notes. It is recommended to read these notes after a version update to see if these changes are relevant to you.

8. Using the algorithm on the Evidencio website

Using the tool on the Evidencio website requires a stable internet connection. The tool was developed to work on the four most commonly used internet browsers; Google Chrome (version 135.0.7049.115 and higher), Mozilla Firefox (version 137.0.2 and higher), Microsoft Edge (version 135.0.3179.98 and higher), and Apple Safari (version 18.4 and higher). The medical device cannot be used in combination with Internet Explorer.

The tool can also be accessed on mobile devices running the most recent versions of the Android (version 15 and higher) and iOS (version 18.4.1 and higher) operating systems.

Correct functioning of the tool with earlier versions of these browsers cannot be guaranteed.

The personal computers, laptops, tablets or smartphones used should at least be able to have an internet connection and use the browsers mentioned above.

Furthermore, the algorithm may be used through the Evidencio iFrame representation of the calculator, as an embedded view, provided that the specific Evidencio guidelines for iFrame implementations of that algorithm are adhered to.

The Evidencio MDSW algorithms can be used with any browser settings that don't distort the regular display of websites, with a 50% to 500% zoom rate, and at a display minimal screen resolution starting from 800x600. However, factory recommended browser settings, 100% zoom rate and regular display resolution are recommended.

The MDSW is intended for authorised users only, and should not be used by unauthorised personnel.

This algorithm is only intended for use in settings where the usage and result of an algorithm are never immediately needed.

8.1. General algorithm landing page

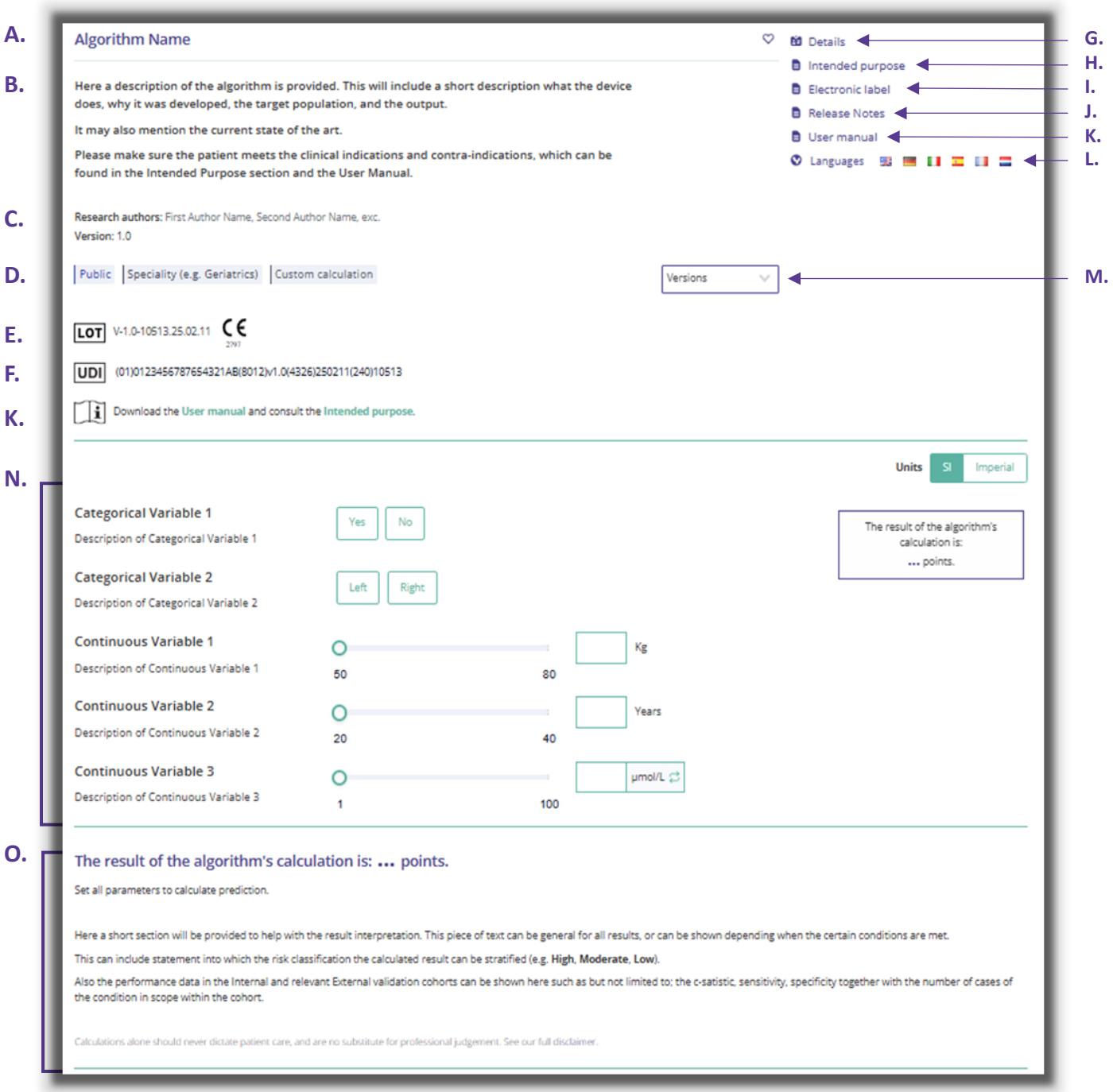

Figure 4. Example of an algorithm landing page on the Evidencio website.

An example of a medical device algorithm interface on the Evidencio platform is shown in **Figure 4**. The different sections indicated are explained in this chapter.

A. Algorithm title

This is the title and name of the algorithm.

B. Algorithm description

This is a short description of the algorithm.

C. Research authors

These are the research authors of the paper that originally published the algorithm.

D. Algorithm tags

These are the tags that are assigned to the algorithm. Evidencio has the following status tags: “Draft”, “Public”, “Private”, “Under review”. Evidencio has the following algorithm type tags: “Composite algorithm”, “Sequential algorithm”, “API algorithm”. Evidencio has the following calculation method tags: “Linear regression”, “Logistic regression”, “Cox regression”, “RScript” and “Custom calculation”. Next to this, there are tags that indicate the specialty e.g. “Cardiology”.

E. LOT number

The LOT number indicated the algorithm version, the algorithm identifier, and the algorithm publication date. Publication date is indicated as YY.MM.DD.

Additionally, the CE mark is displayed next to the LOT number. This way, medical devices can be easily recognized.

F. UDI Number

For information on the UDI Number see **Section 5.2** on **page 5** of this user manual.

G. Details button

On the top right of the algorithm page, several clickable buttons are displayed that show a pop-up when clicked. The first button opens a pop-up concerning additional information about the algorithm. This pop-up has three sections: Details, Study characteristics and Supporting publications & related files.

Details

The first part of the additional information concerns the details of the algorithm as shown in **Figure 5**. This section may show the calculation if it is built as a mathematical formula and, if applicable, shows the conditions at which certain formulas are used.

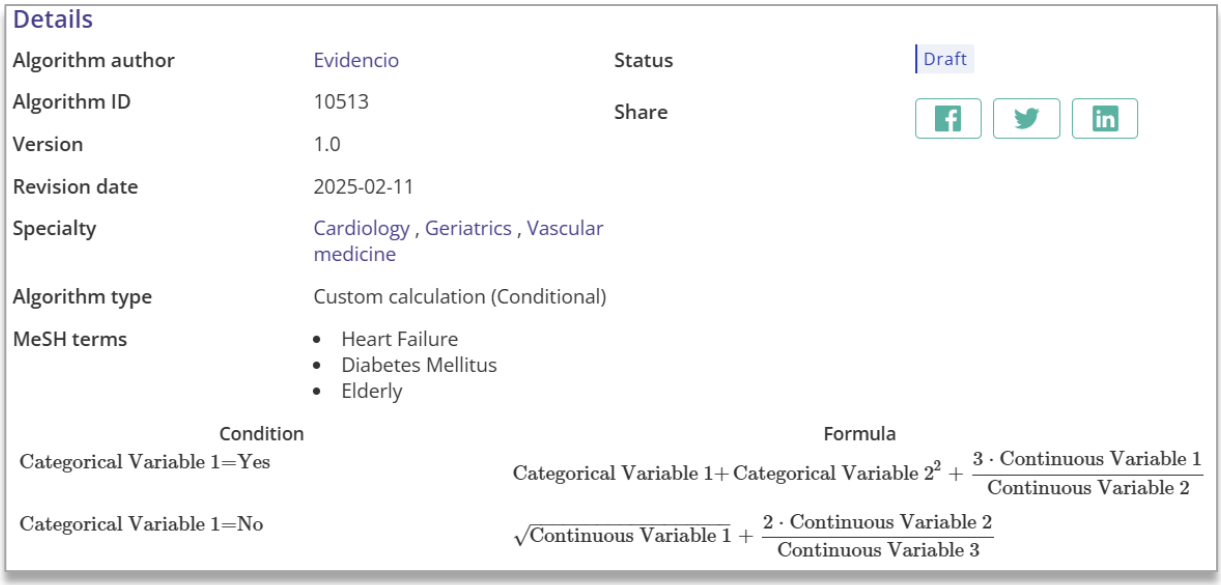

Figure 5. Example of first part of Details section.

Study Characteristics

Below the 'Details section' the section labelled "Study characteristics" provides information on the characteristics of the patient data used to derive and validate the algorithm. Additional information is provided on the methods used to develop and/or validate the algorithm. An example of the Study characteristics section can be seen in **Figure 6**.

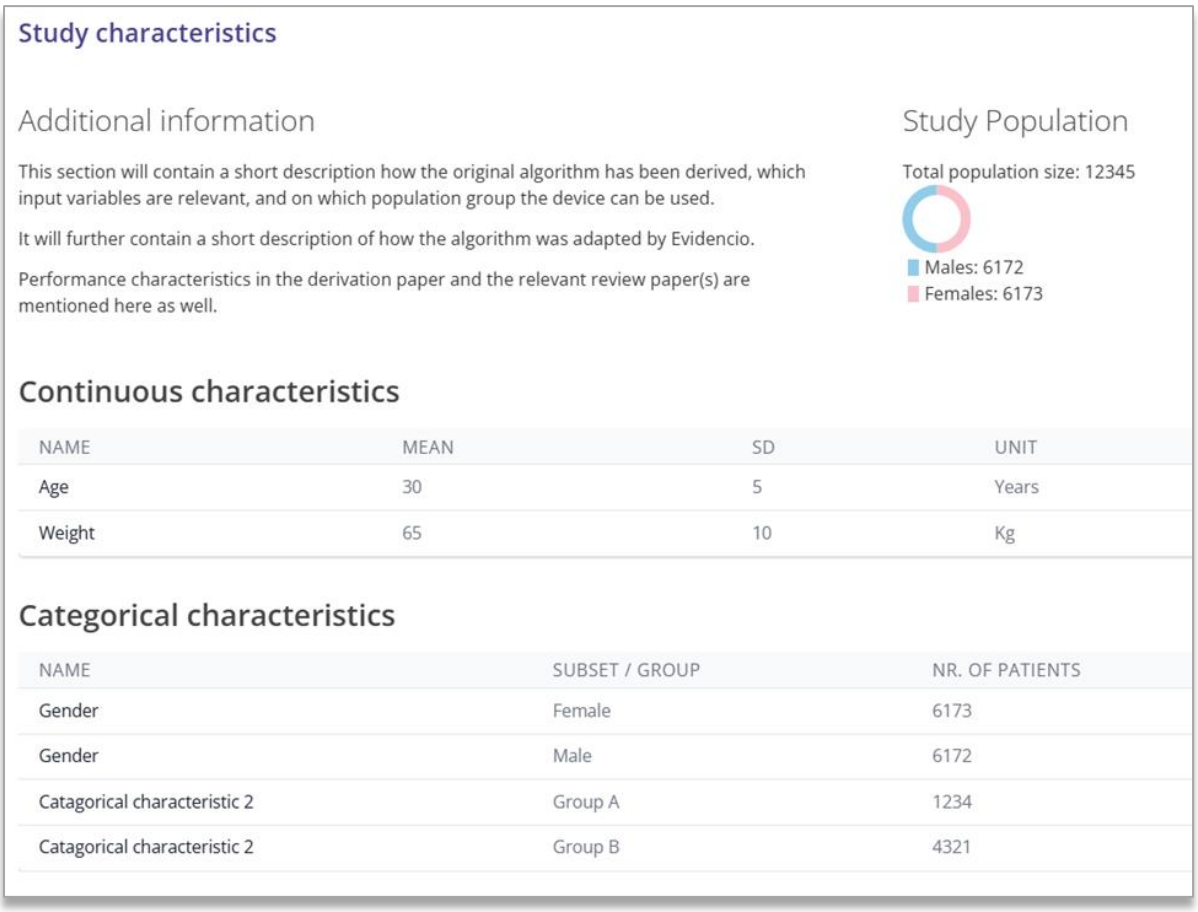

Figure 6. Example of the study characteristics section under the Details tab.

Supporting publications & Related files

An important part of the Study characteristics is the information on Supporting publications and related files. The list of related files and relevant tags can also be found in **Paragraph 7.6**. These sections can be found at the bottom of the Details-pop-up as shown in **Figure 7**.

Figure 7. Example of the Supporting publication & Related files section under the Details tab.

H. Intended purpose

Under this tab, the intended purpose can be found, containing a lot of information regarding the algorithm, its user, target population, clinical benefit, etc. This information is also provided in this manual and can be found in **Chapter 6** on **page 5**.

I. Electronic label

The electronic label button opens a pop-up with the location and address of Evidencio, the LOT number, the UDI number, the CE-mark, the medical device logo and a download link for the declaration of conformity of the medical device. The example of the electronic label is shown in **Figure 8**. The electronic label is unique for each version of the CKD-EPI eGFRcr calculator.

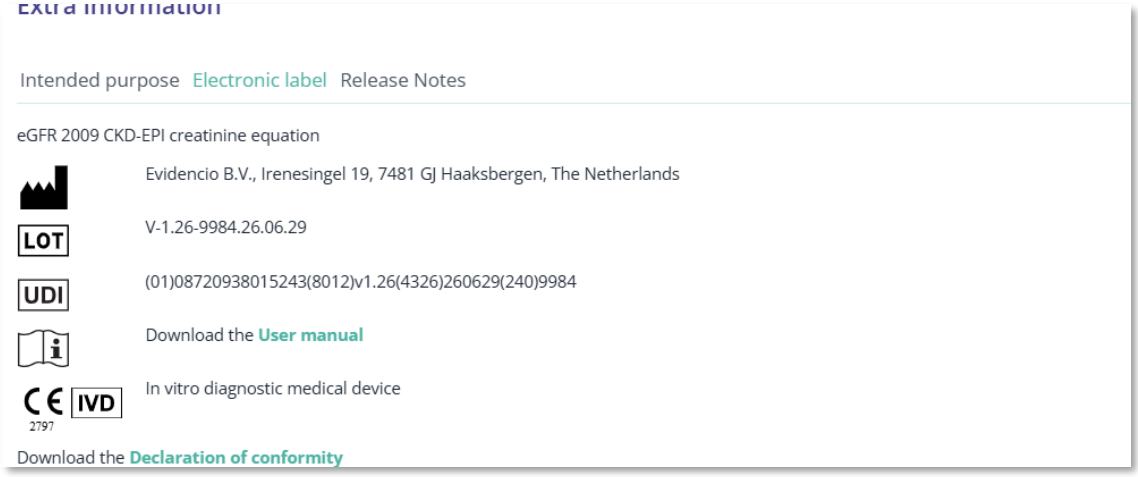

Figure 8. Example of an electronic label under the Electronic Label tab.

J. Release notes

Under this tab the most recent release notes can be found, noting the most significant changes between the versions of the algorithm found on the Evidencio website.

The 'Release Notes' button opens a pop-up with the latest release notes of the algorithm. Here you can find a list of the most significant changes over the different versions of the algorithm. Additionally, if there are any known residual anomalies the user should be aware of, they are listed here. It is recommended to read these notes after a version update to see if these changes are relevant to you.

K. User manual

This user manual can be found in three places: 1) under the short description of the algorithm on the Evidencio algorithm page, 2) on the right of the algorithm page, and 3) as a tab in the electronic label screen. Additionally, all versions of the user manual can be found in the general page for all user manuals for medical devices. The page can be found under the 'About' drop-down menu button as shown in **Figure 9**. The user manual page is shown in **Figure 10.** This version of the manual can be printed if required. If necessary, a paper version of the manual can be requested to be sent to you by mail. Evidencio's contact details are listed in **Chapter 11** of this user manual.

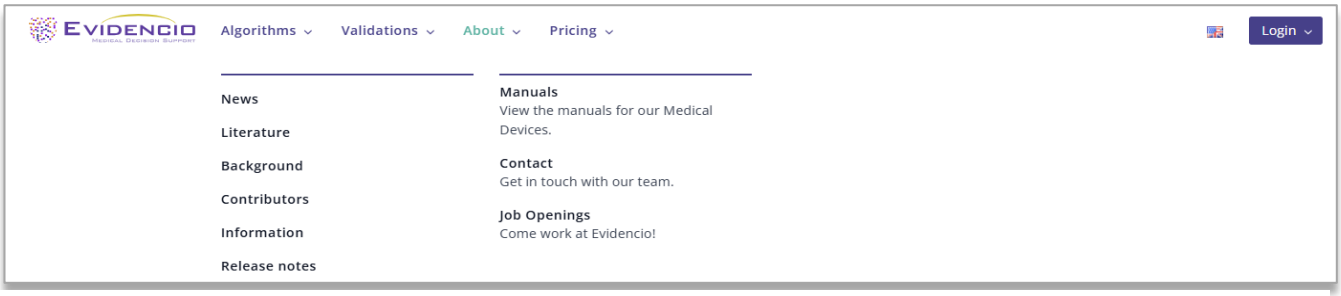

Figure 9. The drop-down menu where the user manual page can be found.

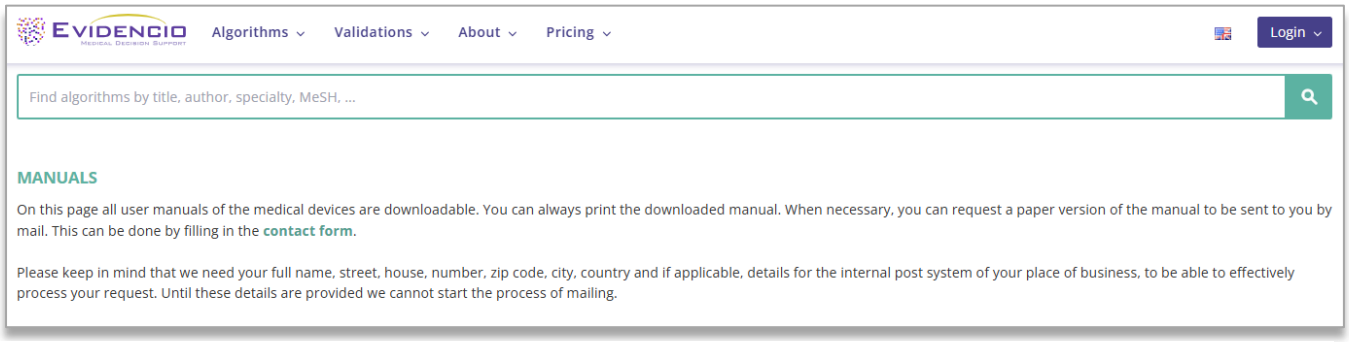

Figure 10. The user manual page for all user manuals.

L. Languages

Here an overview of languages in which the CKD-EPI eGFRcr calculator is available is provided, any of which can be selected by clicking on the corresponding flag icon. The standard language on the Evidencio website is English.

Please note that, if a language is selected, only the user interface of the specific algorithm will be translated, other general features and information on the site might still be set to one of our primary languages English, German, and Dutch.

When you find mistranslations, irregularities, confusing or ambiguous use of language in English or any other language on the Evidencio website or in one of our manuals, please do not hesitate to contact us using the contact information provided at the end of this manual.

M. Algorithm & version selection

Clicking on the Version tab allows the user to select a different version of the algorithm of the CKD-EPI eGFRcr calculator from a list as displayed in **Figure 11**. Please note that the algorithm currently selected is not presented in the dropdown menu.

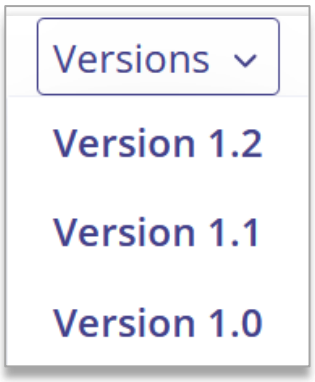

Figure 11. Example of version selection tab.

N. Input section

The Evidencio platform allows two separate input variables; categorical variables and continuous variables.

Categorical variables

In the example shown in **Figure 12** and **Figure 13**, the example **Categorical Variable 1** concerns a categorical variable. The input that is wished to be used can be entered by clicking on either button. The selected button changes to green, as seen in **Figure 13**.

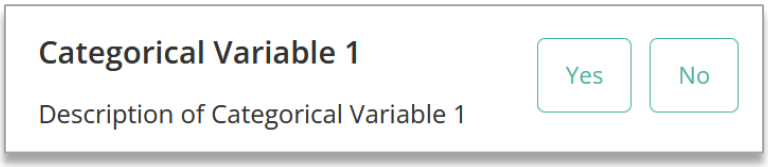

Figure 12. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.

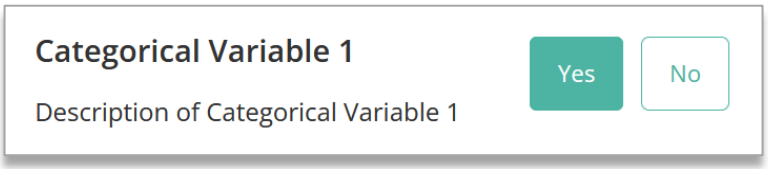

Figure 13. Example of a categorical variable, where the "Yes" button has been clicked.

Continuous variables

In the example shown in **Figure 14**, the **Continuous Variable 3**, exemplifies a continuous variable. The plausible ranges for which the algorithm is tested and deemed valid are used.

The details for a patient can be entered by sliding the button to the correct value, or by entering the correct value in the box on the right-hand side (i.e., where the 10.2 mg/dL is entered for the **Continuous Variable 3**).

Figure 14. Example of a continuous variable, where "10.2 mg/dL" has been entered.

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See **Figure 15** below where the unit has been clicked and switched.

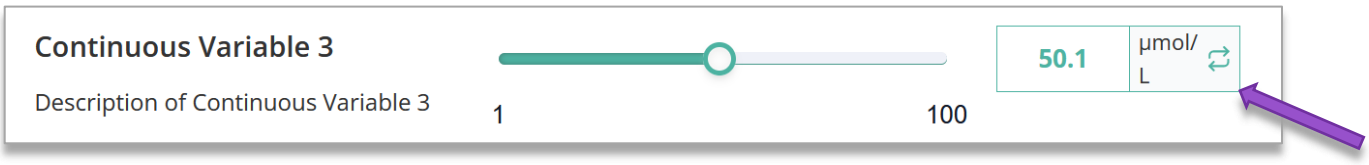

Figure 15. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

Details on variable measurements

Directly underneath the name for each variable, additional details can be provided on, for example, the methods required to enter the correct value for each variable. Details may include but are not limited to; more detailed explanation of the variable, the ranges of the variables (for healthy individuals), or a description when a continuous variable should be true or false (cut-off values).

O. Result section

At the bottom of the algorithm landing page, the results of the algorithm are shown.

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer on: https://www.evidencio.com/disclaimer.

Result calculation

When all variables are filled in, and the user presses calculate, a result can be calculated. No result is displayed until all variables are filled in and the result section will indicate; *"Set all parameters to calculate prediction."*.

Result interpretation

In the result interpretation, a stratification may be provided based on the calculated results. Additional information about this stratification and the classification as found in the derivation and important validation cohorts may also be provided. An example of the information is shown in **Figure 16**.

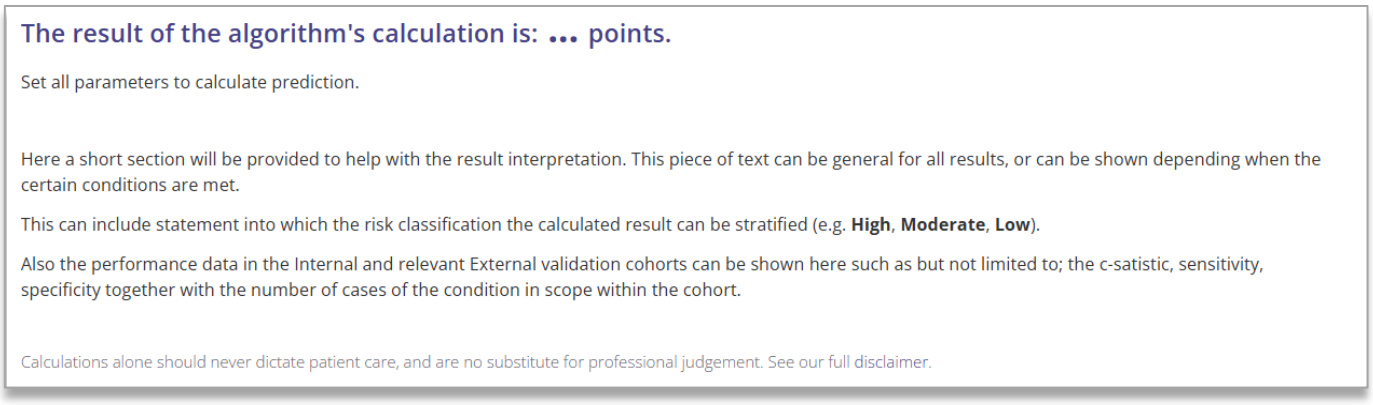

Figure 16. Example of the result display and information section.

9. Implementation of the algorithm through an API

The CKD-EPI eGFRcr calculator can be used through Evidencio's API to allow for (automated) calculation of the score. When using the MDSW through the API, the user should take into account the different inputs for the algorithm, in order to properly interpret the results.

The information provided over the API is the same as the information that is displayed in the graphical user interface on the web application provided by Evidencio. In **Box 1** below, an example of a result from the CKD-EPI eGFRcr calculator over the API is shown. The result concerns a JSON formatted text. The API for the device leverages the generic API that is provided for the Evidencio platform and therefore contains information that may be applicable for different software algorithms and devices. This means that not all of the details provided over the API may be relevant for the current device.


```
{
   "CIPercentage": 0,
   "id": 9984,
   "author": "Evidencio",
   "title": "eGFR 2009 CKD-EPI creatinine equation (without race)",
   "variables": {
      "9136418694": 0.7,
      "9944031449": 55,
      "7205688981": 1.5
   },
   "min": 51.38,
   "max": 51.38,
   "additionalResultSet": [],
   "mintxt": "51.38",
   "maxtxt": "51.38",
   "result": "51.38",
   "resultText": "Estimated GFR:",
   "postresultText": "mL/min/1.73m^2",
   "formulaSegments": [],
   "conditionalResultArray": [
      "<p><p>GFR between 45 and 60 mL/min/1.73m<sup>2 </sup>corresponds to the following KDIGO GFR category:</p><p>G3a: Mildly to Moderately Decreased.</p></p>"
   ],
   "conditionalResultText": "<p><p>GFR between 45 and 60 mL/min/1.73m<sup>2 </sup>corresponds to the following KDIGO GFR category:</p><p>G3a: Mildly to Moderately Decreased.</p></p>",
   "UDI": "(01)08720938015250(8012)v2.1(4326)260626(240)9984",
   "medicalDevice": "This is an in vitro diagnostic medical device. The electronic label is available at: https://www.evidencio.com/models/show/9984?v=2.1",
   "userManual": "Always refer to the user manual for correct use of the in vitro diagnostic medical device. The user manual can be found at: https://www.evidencio.com/manuals"
}
```


Box 1: Example of an API output for CKD-EPI.

Table 6 shows a match between the separately listed items in the API output with the items listed on the graphical user interface on the Evidencio website (elaborated in chapter 8).

Table 6. Correspondence between the API output and user interface on the Evidencio website.

API Item	GUI item	Comment
CIPercentage	N/A	Not applicable for CKD-EPI eGFRcr Calculator as this feature is not used
id	Algorithm ID under 'details' Id used in the URL (www.evidencio.com/models/show/6094)	The ID is the Evidencio specific identification number of the algorithm.
author	Algorithm author under 'details'	Name of the Evidencio user who created the algorithm on the Evidencio platform.
title	Title of the algorithm (part A of figure 1).	-
variables	Input variables and their entered value. (part N. of figure 1)	The API displays the variables as unique IDs.
min	N/A	Depicts the lowest value when the result of the algorithm is a range. Since the CKD-EPI eGFRcr calculator always displays a single value as a result, this value is the same as the 'result'.
max	N/A	Depicts the highest value when the result of the algorithm is a range. Since the CKD-EPI eGFRcr calculator always displays a single value as a result, this value is the same as the 'result'.
additionalResultSet	N/A	N/A
mintxt	N/A	Same as 'min', but as a string.
maxtxt	N/A	Same as 'max', but as a string.
result	The main result of the algorithm, the CKD-EPI eGFRcr calculator score.	-
resultText	The text displayed in front of the main result	e.g. "Estimated GFR".
postresultText	The text displayed behind the main result	e.g. "ml/min/1.73m^2".
formulaSegments	N/A	N/A
conditionalResultArray	Result interpretation displayed beneath "Conditional Information" (section O. in figure 1).	The API result shows the raw HTML text that is rendered by the software used for the graphical user interface.
conditionalResultText	Result interpretation displayed beneath "Conditional Information" (section O. in figure 1).	This section is the same as *'conditionalResultArray',* but displayed as a single string.
UDI	Same as the UDI displayed in the GUI (section F. in figure 1).	-
medicalDevice	The electronic label (section I. in figure 1).	The API refers to the electronic label on the graphical user interface.
userManual	The user manual (section K. in figure 1).	The API refers to the location of the user manual at the user interface & Evidencio website).

Instructions on how to implement the API within a system are included in a separate document that is made available to the party performing the technical implementation. The party performing the integration of the CKD-EPI eGFRcr calculator using the API should adhere to the requirements outlined in **9984-DOC-45 instructions for API integration CKD-EPI eGFRcr calculator.**

10. User manual revision history

Version	Revision notes
V1.0	First version for publishing as IVDR device.
V2.0	Changes to the intended purpose and addition of statement on the Summary of Safety and Performance
V3.0	Updated with newest versions after adding multiple languages Updated the manufacturer address

11. Manufacturer details

Contact details of Evidencio:

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tel: +31 53 85195 08
e-mail: info@evidencio.com