User manual

for the

CKD-EPI eGFRcr calculator

eGFR 2009 CKD-EPI creatinine equation
eGFR 2009 CKD-EPI creatinine equation (without race)
eGFR 2021 CKD-EPI creatinine equation

Version 4, September 2024, in English

Table of Contents

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).

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

2. Disclaimer

Evidencio provides information, models, calculators, equations, and algorithms (tools) intended for use by healthcare professionals. Some of these tools have been certified as CE-medical devices. For such CE-marked content the 'Official Legal Disclaimer for CE-marked content' applies. All other content and tools provided by Evidencio are explicitly only covered by the 'Official Legal Disclaimer for non CE-marked content. Both are available on the Evidencio website: https://www.evidencio.com/disclaimer.

3. Warnings

3.1. Warnings for CE-marked content

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Calculations alone should never dictate patient care, and are no substitute for professional judgement. This tool is only to be used by professionals in a clinical setting, 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 in **paragraphs 6.3.1** and **6.3.2** 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 model is only intended for use in settings where the usage and result of a model are never immediately needed.

The data used to perform the calculations is stored by Evidencio to enhance model 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.

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.

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 model 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 model.

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

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

a) The risk calculation was wrong or;
b) The MDSW prediction model 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 focused on reducing the risks' probability and severity. Concluding that the risks could not be mitigated further, the residual risks were classified as *low-level and acceptable.* It should be noted that the use of Evidencio's Medical Device Software is itself a risk mitigation measure, as Evidencio's certified Quality Management System ensures and monitors the reliability of the calculations performed with its certified medical devices.

The CKD-EPI eGFRcr calculator does not have any direct side effects relevant for the patient.

5. Electronic Label

The electronic label of this device contains the following information:

Name of the device: CKD-EPI eGFRcr calculator

Manufacture information: Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands

LOT number

eGFR 2009 CKD-EPI creatinine equation:	V-1.25-9984.24.09.12
eGFR 2009 CKD-EPI creatinine equation (without race):	V-2.0-9984.24.09.12
eGFR 2021 CKD-EPI creatinine equation	V-3.0-9984.24.09.12

UDI-PI number:

eGFR 2009 CKD-EPI creatinine equation:	(01)08720938015243(8012)v1.25(4326)240912(240)9984
eGFR 2009 CKD-EPI creatinine equation (without race):	(01)08720938015250(8012)v2.0(4326)240912(240)9984
eGFR 2021 CKD-EPI creatinine equation:	(01)08720938015267(8012)v3.0(4326)240912(240)9984

The electronic label can be found on the Evidencio website, see also **Section I** in **chapter 10** of this manual.

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 indicated the model version, the model identifier, and the model publication date. Publication date is indicated as YY.MM.DD.

5.2. UDI-PI number

Stands for Unique Device Identifier Production Identifier (UDI-PI) number is an international tool that helps users identify and find information on products. Evidencio's UDI-PIs 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-PI, is linked to one of the 3 device sub-models. Version 1.25 for eGFR 2009 CKD-EPI creatinine equation, Version 2.0 for eGFR 2009 CKD-EPI creatinine equation (without race), and Version 3.0 for eGFR 2021 CKD-EPI creatinine equation.

6. Intended Purpose

6.1. Intended Medical 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.

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 qualified medical specialists only. The device is not intended for use by patients on their own.

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 patients with 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 algorithm positively impacts patient management by allowing for the estimation of Glomerular Filtration Rate with a singular blood test, which estimates Renal function, informing clinical management on further *diagnostic/prognostic/therapeutic* options and strategies, and avoiding expensive, invasive or burdensome tests to measure GFR.
- Digital implementation of the algorithm underlying the CKD-EPI eGFR equation as a medical device can improve the speed and reliability of calculation.

6.3. Indented 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 Indications

The CKD-EPI eGFRcr calculator should be used for patients who are 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 CKD-EPI eGFRcr calculator is intended to be used by Healthcare Professionals or automatically calculated through Evidencio's API. Results shall always be reviewed and interpreted by qualified medical specialists only, 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, and on the mobile app provided by Evidencio. The MDSW can also be used through Evidencio's iFrame representation as an embedded view, provided that the specific Evidencio guidelines for iFrame implementations of this MDSW are adhered to. 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.

6.6. Physical Interaction

The current version of the MDSW concerns 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. 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. Result interpretation

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.

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

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

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

8. Additional information

8.1. Details

Model author wrvandijk

Root model ID 9984

	Version number	Revision date
eGFR 2009 CKD-EPI creatinine equation	1.25	13 September 2024
eGFR 2009 CKD-EPI creatinine equation (without race)	2.0	13 September 2024
eGFR 2021 CKD-EPI creatinine equation	3.0	13 September 2024

Speciality Nephrology

Model type Custom

MeSH terms

- Kidney
- Creatinine
- Glomerular Filtration Rate

8.2. Input variables

To perform the calculation, the CKD-EPI eGFRcr calculator requires the input variables as listed in the table below.

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 (eGFR 2009 CKD-EPI creatinine equation)	Categorical	Black/Non-Black	*N/A*
Serum Creatinine	Serum Creatinine level	Continuous	0.1-25 (0.1)	*mg/dL*
			10-1000 (1)	*µmol/L*

8.3. 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 1. 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 3. The Conditions and Formula of the eGFR 2021 CKD-EPI creatinine equation.

8.4. 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.

In the tables 1 and 2, information on the characteristics of the patient data used to derive and validate the model is provided.

Table 1. This table contains information on the patient group data used to derive the model.

NAME	MEAN	SD	UNIT
Age	47	14.8	Year
BMI	28.2	6.1	kg/m2
Measured GFR	67.6	39.6	ml/min/1.73m^2
Creatinine	1.66	1.16	mg/dl

Table 2. This table contains categorical characteristics on the patient group data used to derive the model.

NAME	SUBSET / GROUP	NR. OF PATIENTS
Age	<40yr	2921
Age	40-65 yr	4309
Age	>65 yr	1024
BMI	<20	285
BMI	20 to <25	2446
BMI	25 to <30	2923
BMI	≥30	2600
Diabetes (data available for 3616 patients)	Yes	2406
Kidney-donor candidate	Yes	1030
Measured GFR Category	<30 ml/min/1.73 m2	1722
Measured GFR Category	30 to <60 ml/min/1.73 m2	2334
Measured GFR Category	60 to <90 ml/min/1.73 m2	1669
Measured GFR Category	≥90 ml/min/1.73 m2	2529

8.5. Supporting publication & Related files

Several relevant studies, such as the original derivation study by Levey et al. are contained in **Table 3**. 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 3. 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*

8.6. 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 clicking on Release Notes. It is recommended to read these notes after a version update to see if these changes are relevant to you.

9. Implementation of the model through an API

The CKD-EPI eGFRcr calculator can be used through Evidencio's API to allow for (automated) calculation of the estimated Glomerular Filtration Rate. In the case of use of the MDSW through the API, the user should take into account the different inputs for the model, in order to properly interpret the results. Furthermore, the information contained within this user manual, specifically chapters 3-8, should be read and understood by the user.

Instruction 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.

When using the MDSW through the API, the warnings and descriptions given in this document all apply, as does the additional information. The information for use included in this document regards both use through the website as well as use through the API, as long as the API is properly implemented. The API is only intended for authorized users.

10. Using the model on the Evidencio website

Using the tool on the Evidencio website, requires a stable internet connection. The tool was tested on the following browsers and will run on these versions and higher;

- Personal computers or laptops using the following browsers:
  - Safari (version 17.5 and higher)
  - Chrome (version 126.0.6478.127 and higher)
  - Firefox (version 128.0 and higher)
  - Edge (version 126.0.2592.102 and higher)
- Tablets or smartphones running on the next operating systems:
  - IOS (version 17.5.1 and higher)
  - Android (version 13 and higher)

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

The medical device cannot be used in combination with Internet Explorer. The personal computers, laptops, tablets or smartphones used should at least be able to have an internet connection and use the browsers mentioned above. The minimal screen resolution should be 800x600.

Furthermore, the model 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 model are adhered to.

The Evidencio MDSW models 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 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 model is only intended for use in settings where the usage and result of a model are never immediately needed.

10.1. General model landing page

The medical device model on the Evidencio platform is shown in Figure 4 The model landing page contains the following sections, that are indicated in Figure 4.

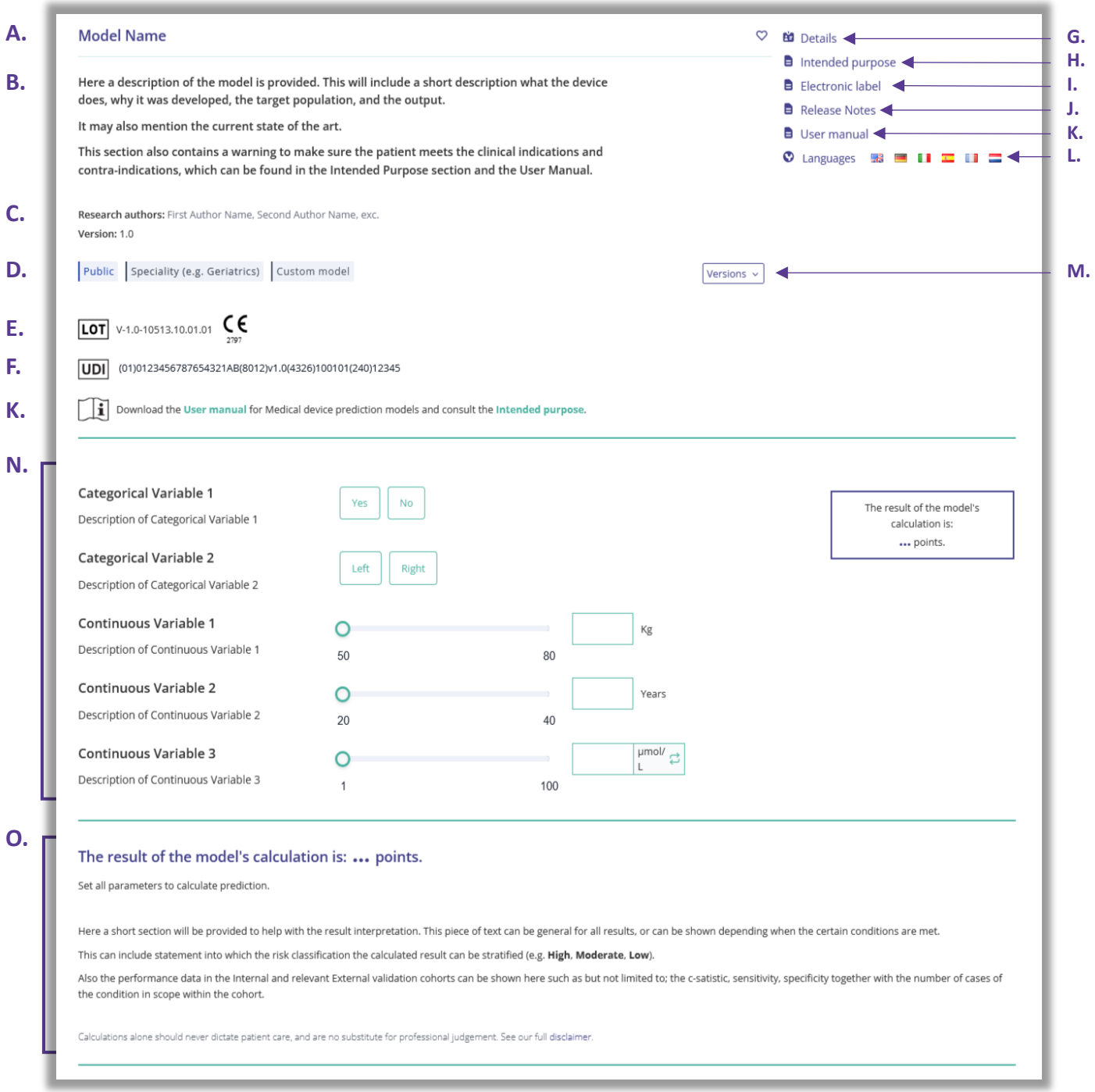

Figure 4. Example of a model landing page on the Evidencio website.

A. Model title

This is the title and name of the model

B. Model description

This is a short description of the model.

C. Research Authors

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

D. Model tags

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

E. LOT number

The LOT number indicated the model version, the model identifier, and the model 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-PI number

For a description of the UDI-PI number; see **section 5.2** on **page 5** of this manual.

G. Details button

On the top right of the model 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 model. 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 model as shown 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.

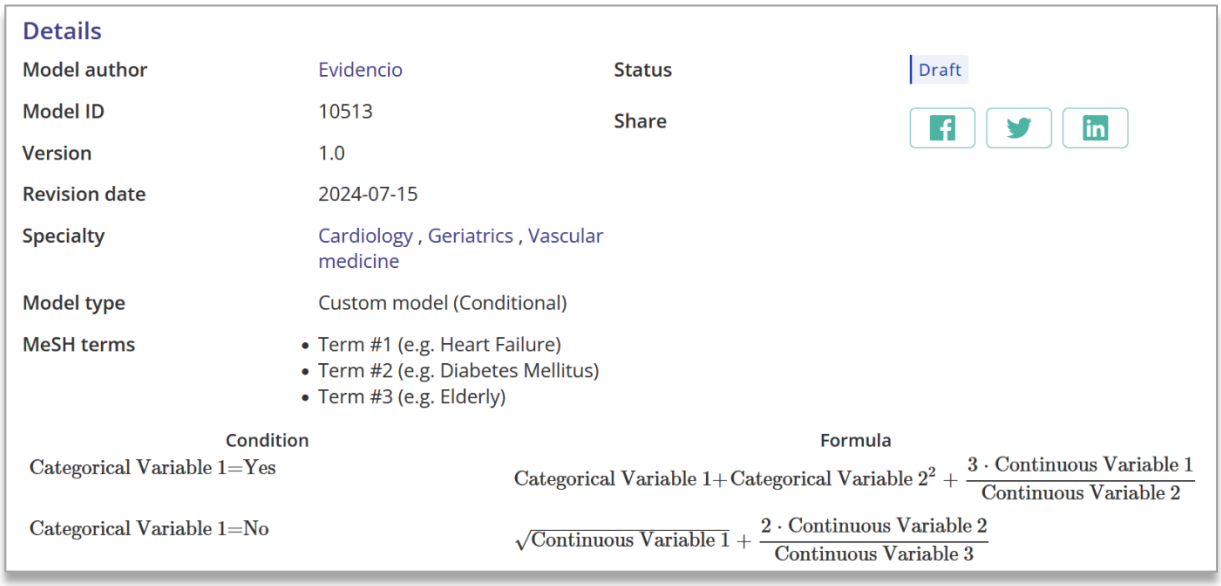

Figure 5. Example of first part of detail section.

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 model. Additional information is provided on the methods used to develop and/or validate the model. An example of the Study characteristics section can be seen in figure 6.

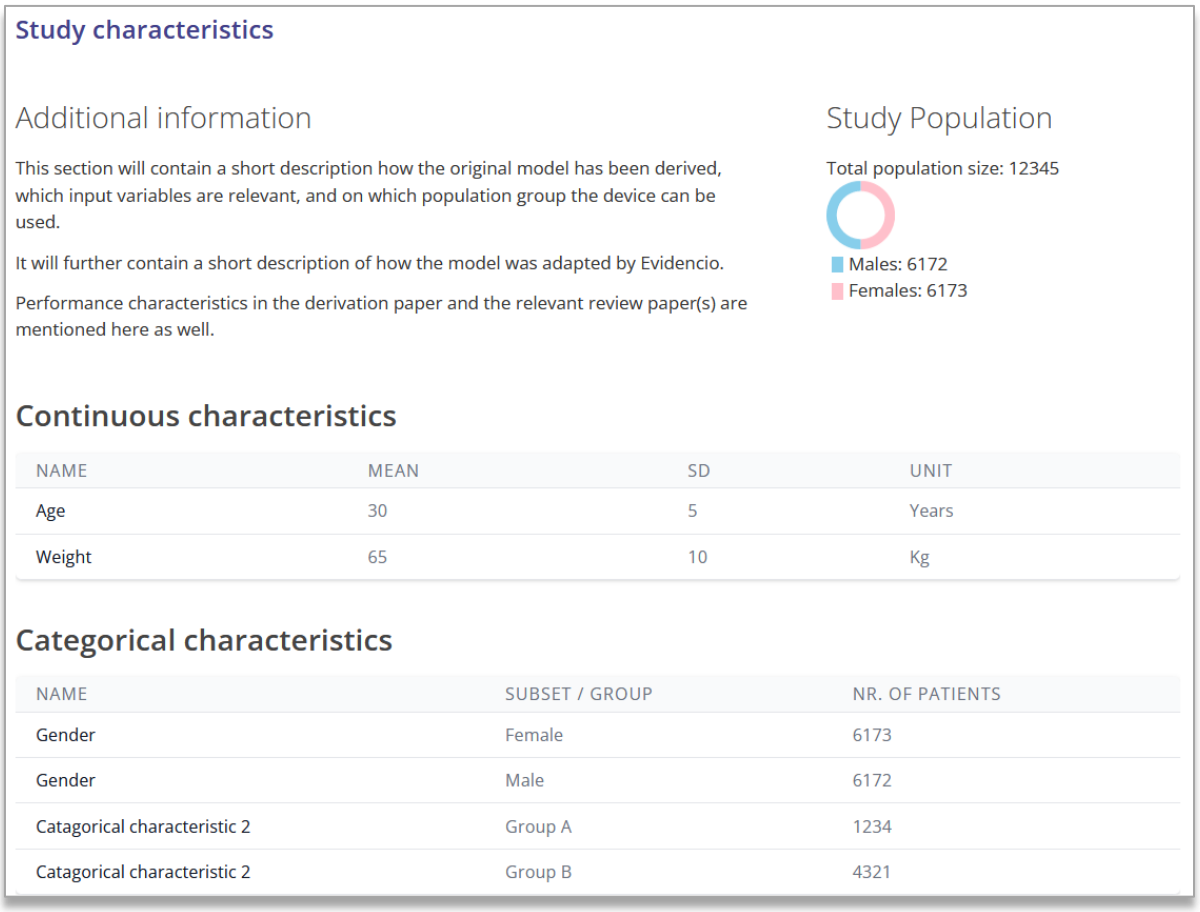

Figure 6. Example of the study characteristics section under the Details tab.

Supporting publications & Related files

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

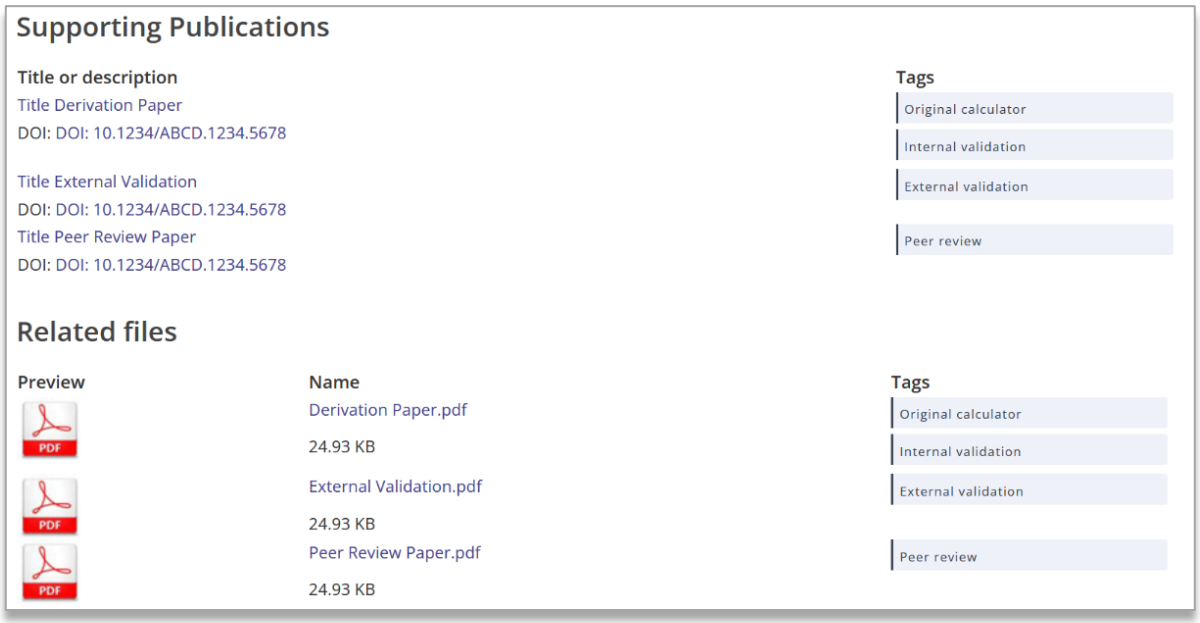

Figure 7. Example of the Supporting publication & Related files section under the Details tab.

Tags are attached to the different files to identify their link with the model. Examples of relevant tags are a.o.; “Peer review”, “Internal validation”, “External validation”, and “TRIPOD”. Publications that have the tags: “Internal validation” or “External validation”, contain the performance characteristics of the device. Figures and tables which help to interpreted the results may also be provided here.

H. Intended purpose

Under this tab, the intended purpose can be found, containing a lot of information regarding the model, 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 model comprising the CKD-EPI eGFRcr calculator.

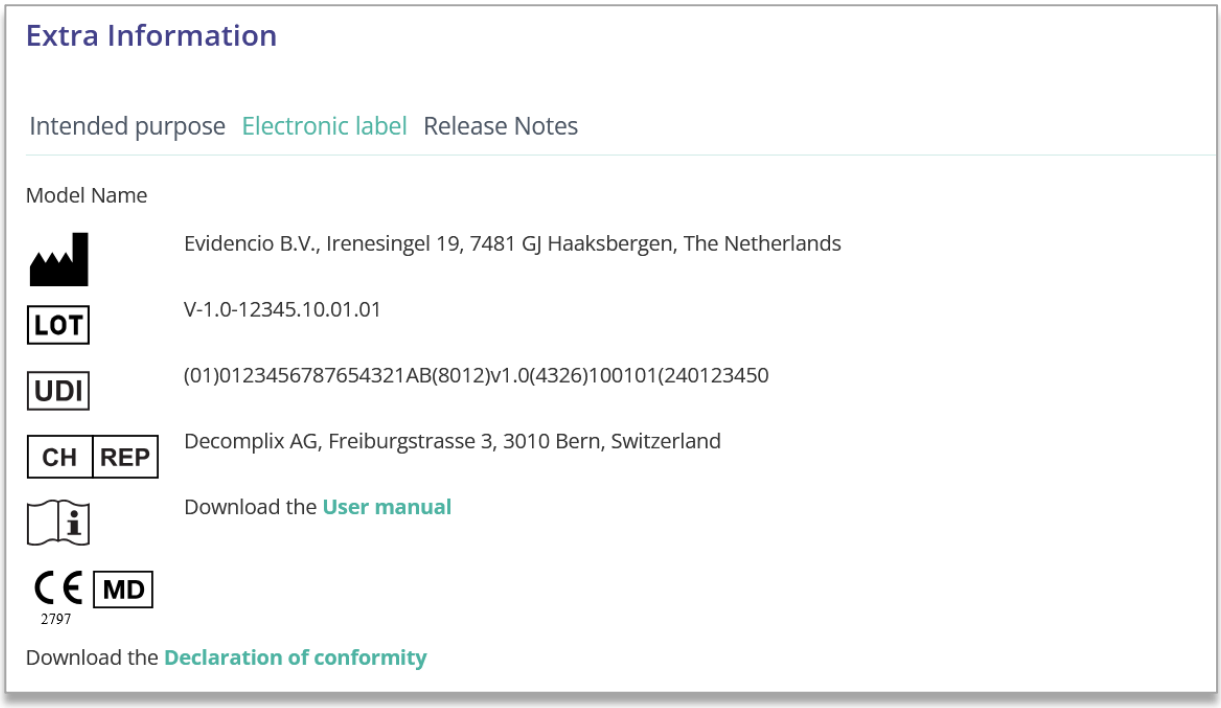

Figure 8. Example of an electronic label under the Electronic Label tab.

J. Release notes

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

The ‘Release Notes’ button opens a pop-up with the latest release notes of the model. Here you can find a list of the most significant changes over the different versions of the model. 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 model on the Evidencio model page, 2) on the right of the model 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 **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.

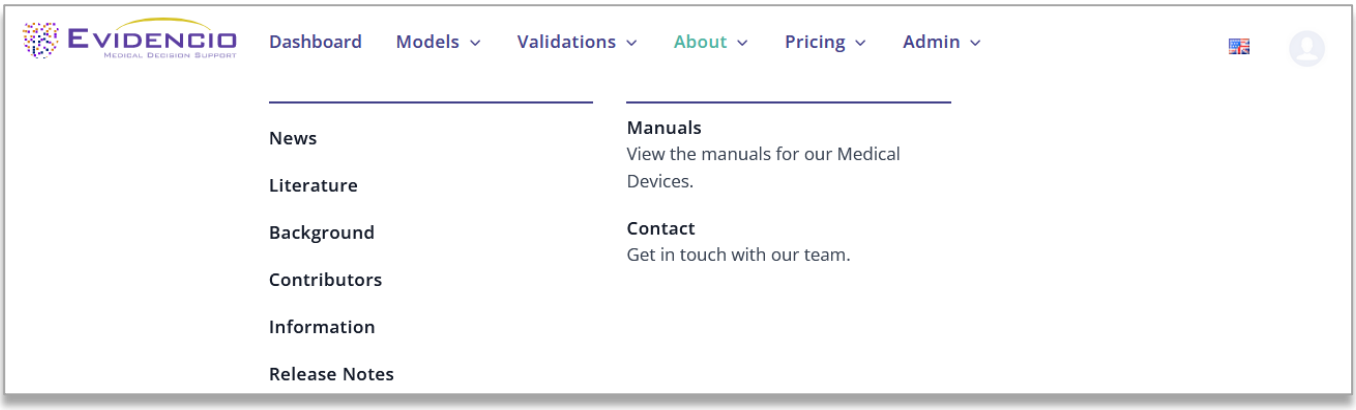

Figure 9. The drop-down menu where the user manual page can be found.

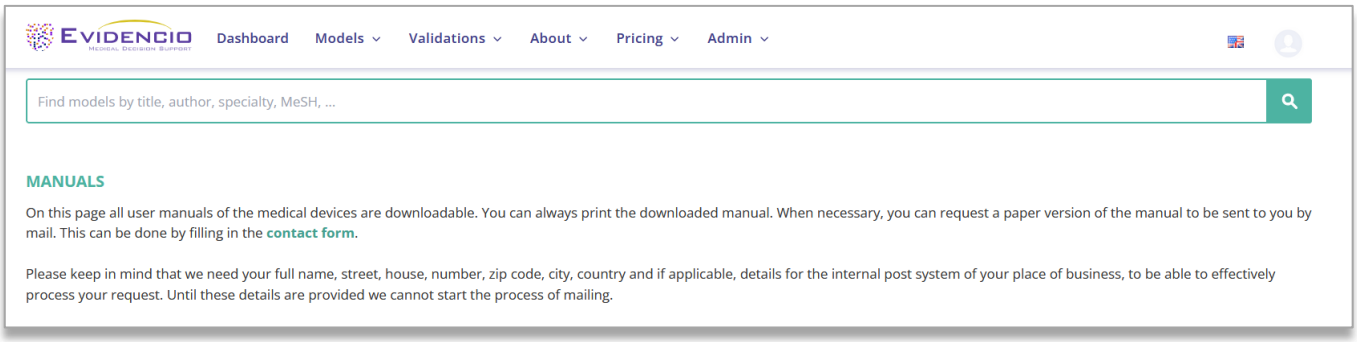

Figure 10. The user manual page for all user manuals.

L. Languages

The standard language on the Evidencio website is English. When other languages are available, these can be selected here. The list of languages may be different between models and may change when in time more languages will become available. Currently the CKD-EPI eGFRcr calculator and its user manual are available in English.

Please note that, if a language is selected, only the user interface of the specific model 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, or 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. Model & Version selection

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

Figure 11. Example of the model 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 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**.

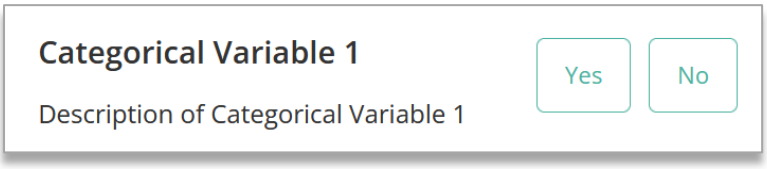

Figure 12. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.

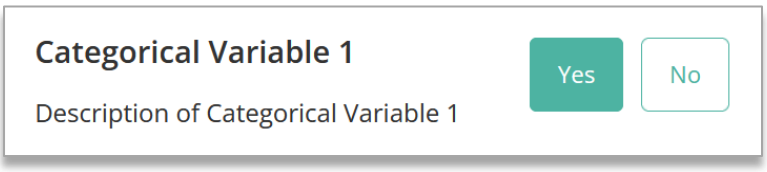

Figure 13. Example of a categorical variable, where the "Yes" button has been clicked.

Continuous variables

In the example shown in **Figure 14**, the **Continuous Variable 3**, exemplifies a continuous variable. The plausible ranges for which the model 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**).

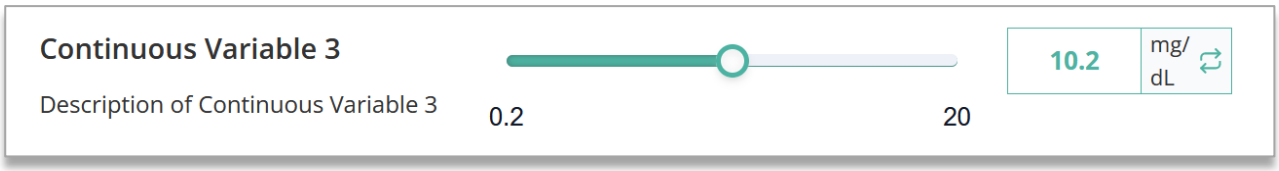

Figure 14. Example of a continuous variable, where "10.2 mg/dL" has been entered.

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See figure 14 below where the unit has been clicked and switched.

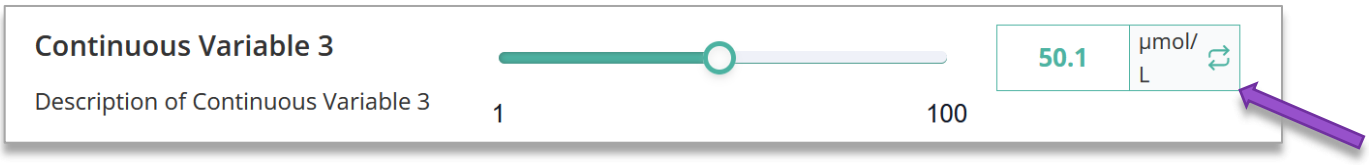

Figure 15. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

Details on variable measurements

Directly underneath the name for each variable, additional details can be provided on 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.

O. Result section

At the bottom of the page, the results of the model 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, a result will be calculated. No results 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, an estimated GFR based on creatinine is given. Additional information about this value and the associated health condition as found in the derivation and important validation cohorts may also be provided. An example of the information is shown in **Chapter 7**.

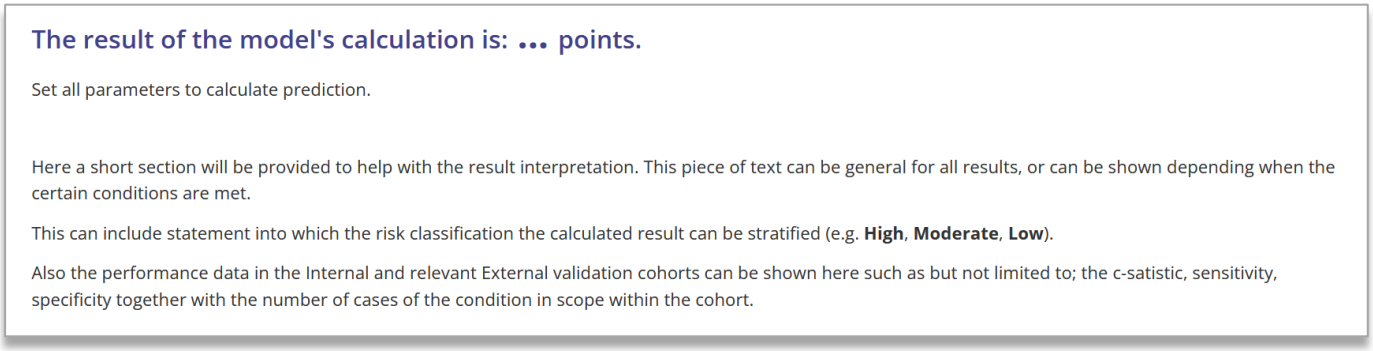

Figure 16. Example of the result display and information section.

11. Manufacturer details

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.

Contact details of Evidencio:

Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
www.evidencio.com
tel: +31 53 85195 08
e-mail: info@evidencio.com