User manual for the SCORE2

Version 3, November 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 SCORE2. 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

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

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

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 SCORE2

This model estimates the 10-year risk of cardiovascular disease events (both fatal and non-fatal) in European patients.

The model includes three different equations:

The **SCORE2**, intended for apparently healthy patients between 40 and 69 years old.

The **SCORE2-OP**, intended for apparently healthy patients (including T2DM) 70 years or older

The **SCORE2-Diabetes**, intended for patients with Type 2 Diabetes Mellitus, between 40 and 69 years old.

The SCORE2 algorithms include the use of risk regions to estimate cardiovascular risk, based on the regional baseline risk for the patient. The country of the patient can be selected within the model.

4.1. Lifetime, residual risks and side effects

The SCORE2 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 SCORE2 is a low-risk device, there are no noticeable risks involved outside of possible mis-estimation of patient 10-year fatal & non-fatal cardiovascular disease risk, 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 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 inaccessibly 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-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 SCORE2 does not have any direct side effects.

5. Electronic Label

The electronic label of this device contains the following information:

Name of the device	SCORE2
Manufacture information	Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
LOT number	V-1.18-2570.24.10.18
UDI-PI number	08720938015281

The electronic label can be found on the Evidencio website, see also section **I** and **Figure 5**.

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.

6. Intended Purpose

6.1. Intended Medical Use

The SCORE2 is intended to be used by healthcare professionals who are capable of operating the device and interpreting its results. It can be used to estimate the 10-year fatal & non-fatal cardiovascular disease risk.

The SCORE2 comprises the SCORE2, SCORE2-Diabetes and SCORE2-OP for Older Patients (SCORE2-OP) algorithms.

The SCORE2 algorithm combines sex, age, geographical location, systolic blood pressure, smoking status, total cholesterol, and HDL-cholesterol to provide an estimate on the 10-year fatal & non-fatal cardiovascular disease in apparently healthy individuals. For the SCORE2-OP, Diabetic status (T2DM) is also included in the estimation. The SCORE2-Diabetes also includes Diabetic status, Age at diabetes diagnosis, HbA1c, and eGFR.

The SCORE2 Algorithm is not intended to replace clinical decision-making, it can only provide information to the user on the estimation of the 10-year cardiovascular disease risk. The user can use this information to support clinical decision-making on treatment options. In practice, this typically entails the decision to initiate cardiovascular risk reducing treatment.

6.2. Clinical benefit

The SCORE2 is intended to assist medical professionals with patients that have relevant and specified clinical outcome parameters. Concretely, this is achieved by estimating a risk in order to support clinical decision-making aimed at apparently healthy patients, in order to support clinical decision-making regarding patient prognosis. Correct functioning of the SCORE2 can result in these clinical benefits:

- The SCORE2 can assist in risk stratification for patients
- The SCORE2 aids in the selection of risk reducing treatment, providing preventive measures for cardiovascular disease.
- Digital implementation of the algorithm underlying the SCORE2 as a medical device can improve the speed and reliability of calculation. This would further increase the accuracy of the prognosis and by extent increase the chance for the above-mentioned benefits.

6.3. Indented target population and exclusion

The SCORE2 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 SCORE2 should be used for patients who meet the following inclusion criteria:

- Aged 40 years or older
- One of the following:
    - Apparently healthy
    - Patients with type 2 diabetes mellitus

6.3.2. Clinical contra-indications

The SCORE2 should not be used for patients who meet one or more of the following exclusion criteria:

- Established atherosclerotic cardiovascular disease
- If diagnosed with diabetes:
    - Severe Target Organ Damage (TOD)
    - Symptomatic ASCVD

- Specific risk factors:
    - Chronic Kidney Disease
    - Familial Hypercholesterolemia
    - Genetic/rarer lipid disorders
    - Blood pressure disorders
    - Pregnancy

6.4. User profile

The SCORE2 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 professionals 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 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 version of the SCORE2 Algorithm concerns the initial version of MDSW of which Evidencio is the manufacturer.

6.8. Functioning, physical principle

The MDSW's underlying mathematical formula is a cox regression model, aimed at providing a cumulative risk estimate over the next 10-years. The acquisition and processing of the data, the analyses to assemble the relevant criteria for the MDSW and the set up and refinement of the SCORE2 Algorithm are provided in the instructions for use. Entering the details for an individual in the MDSW initiates the estimation of 10-year cardiovascular disease risk.

7. Result interpretation

The outcome of the MDSW is a 10-year risk of fatal or non-fatal CVD, as well as a corresponding risk class based on 10-year estimated risk, patient age, and diabetes status, in accordance with the 2021 ESC guidelines and the 2023 ESC Diabetes guidelines.

The primary output of this device is given as;

Expected 10-year CVD event risk (fatal and non-fatal): [#] % (adjusted for region, age group, and sex)

Conditional information

The most recent ESC guidelines stratify patients into different risk categories depending on their age and calculated risk, an overview of which is provided in **Table 1** below.

Table 1. Risk stratification of patients with and without type 2 diabetes mellitus based on their age group and calculated risk according to the most recent ESC guidelines. For patients without T2DM <69 years, no distinction is made between low and moderate risk.

	Patients without type 2 diabetes mellitus			Patients with type 2 diabetes mellitus	
	<50 years	50-69 years	>70 years	<70 years	>70 years
Low risk	<2.5%	<5%	<7.5%	<5%	<7.5%
Moderate risk				5% - 10%	
High risk	2.5% - 7.5%	5% - 10%	7.5% - 10%	10% - 20%	7.5% - 10%
Very high risk	<7.5%	>10%	>20%	>20%	>20%

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:	Dr. R.G. Pleijhuis
Root model ID	2570
Version	1.18
Revision date	18-Oct-2024
Speciality	Cardiology, Intensive care
Model type	R-Script model
MeSH terms	• Cardiovascular Diseases

8.2. Input variables

To perform the calculations successfully, the SCORE2 requires the input variables as listed in **Table 2**. The first variable produces a drop-down menu in which the risk region can be selected. The risk regions and their corresponding risk classification are displayed in **Table 3**.

Table 2. Variables used as input for the SCORE2.

Name	Description	Type	Range (step size)	Units
Region	The region in which the patient resides	Categorical	[See list of countries in **Table 3**]	-
Age	The age of the patient	Continuous	40 – 100 (1)	Year
Sex	The sex of the patient	Categorical	Male Female	-
Current smoking	The smoking status of the patient	Categorical	No Yes	-
SBP	The Systolic Blood Pressure of the patient	Continuous	100 – 200 (1)	mmHg
Total cholesterol	Total Cholesterol of the patient	Continuous	1.5 – 1.0 (0.1)	mmol/L
			59.0 – 386.0 (0.1)	mg/dL
HDL cholesterol	HDL cholesterol of the patient	Continuous	0.5 – 4.5 (0.1)	mmol/L
			20.0 – 174.0 (0.1)	mg/dL
Type 2 Diabetes Mellitus	Whether or not a patient has Type 2 Diabetes Mellitus	Categorical	No Yes	-
Age at diabetes diagnosis	Patient age at the diagnosis of diabetes	Continuous	0 - 69 (1)	Year
HbA1c	Blood haemoglobin A1c levels	Continuous	1.0 – 200.0 (0.1)	mmol/mol
			2.5 – 20.0 (0.1)	%
eGFR	Estimated Glomerular Filtration Rate of the patient	Continuous	0 – 200 (1)	mL/min/1.73m^2

Table 3. List of selectable countries and their corresponding designated risk region.

Low risk region	Moderate risk region	High risk region	Very high risk region	
France	Iceland	Albania	Armenia	Republic of Moldova
Israel	Portugal	Czech Republic	Lithuania	Ukraine
Spain	Sweden	Turkey	Georgia	Kyrgyzstan
Netherlands	Italy	Kazakhstan	Latvia	Uzbekistan
Switzerland	San Marino	Croatia	Serbia	Egypt
Denmark	Ireland	Poland	Romania	Morocco
Norway	Cyprus	Estonia	Montenegro	Syria
Luxembourg	Finland	Slovakia	Russian Federation	Tunisia
Belgium	Austria	Hungary	TFYR Macedonia	Lebanon
United Kingdom	Malta	Bosnia and Herzegovina	Belarus	Algeria
	Greece		Azerbaijan	Libya
	Germany		Bulgaria	

Formula

The SCORE2 is composed of three Cox-regression models, with separate equations for younger (40-69 years old), older (70+) and diabetic patients. The equations can also be found in the original 2021 and 2023 derivation papers by the ESC Cardiovascular risk collaboration and the SCORE2 working group, SCORE2-OP working group, and SCORE2-Diabetes working group.

8.3. Study characteristics

8.3.1. SCORE2

The SCORE2 working group which presented the SCORE2 model in their 2021 paper, described the derivation as follows;

"For model derivation, we used individual-participant data from 44 cohorts included in the Emerging Risk Factor Collaboration (ERFC) and the UK Biobank (UKB). The ERFC has collated and harmonized individual-participant data from many long-term prospective cohort studies of CVD risk factors and outcomes. Prospective studies in the ERFC were included in this analysis if they met all the following criteria: had recorded baseline information on risk factors necessary to derive risk prediction models (age, sex, smoking status, history of diabetes mellitus, systolic blood pressure, and total- and HDL-cholesterol); were approximately population-based [i.e. did not select participants on the basis of having previous disease (e.g. case-control studies) and were not active treatment arms of intervention studies]; had a median year of baseline survey after 1990; and had recorded cause-specific deaths and/or non-fatal CVD events (i.e. non-fatal myocardial infarction or stroke) for at least 1-year of follow-up."

Countries were stratified into Low, moderate, high, or very high-risk region groups based on their CVD mortality rates. This was used to include an additional risk factor which partially captures the background risk for CVD experienced by the individuals in those regions. This variable is used in all models comprising the SCORE2.

In **Table 4** and

Table 5 information on the characteristics of patient data used to derive and validate the model is provided.

Table 4. This table contains information on the patient group data used to derive the SCORE2 model.

Name	Mean	SD	Unit
Age (years)	57	9	Years
Systolic blood pressure	136	19	mmHg
Total cholesterol	5.8	1.1	mmol/L
HDL-cholesterol	1.4	0.4	mmol/L

Table 5. This table contains categorical characteristics on the patient group data used to derive the SCORE2 model.

Name	Number of patients
Total number of participants	677,684 (44% male)
Current smoker	101,211 (15%)
Diabetes mellitus	31,413 (5%)
Non-cardiovascular deaths	33,809

After model derivation, the model was externally validated in 25 contemporary cohorts with a total of 1,133,181 individuals form 15 countries. The discrimination of the derivation dataset was good, with a C-index of 0.739 (95% CI 0.736-0.741). The external validation yielded C-indices ranging from 0.67 (0.65-0.68) to 0.81 (076-0.86).

8.3.2. SCORE2-OP

The SCORE2-OP working group presented the SCORE2-OP in their 2021 paper. Here they described the derivation through a recalibration of the SCORE2 algorithm, described in their paper as follows;

"The study design is closely related to the new SCORE2 model that estimates 10-year fatal and non-fatal CVD risk in individuals without previous CVD or diabetes aged 40–69 years. The model coefficients were derived in the Cohort of Norway (CONOR) study. A total of 10089 non-fatal and fatal CVD events occurred in 305640 person years of follow-up in the 28503 participants included from the CONOR study."

In **Table 6** and **Table 7** information on the characteristics of patient data used to derive and validate the model is provided.

Table 6. This table contains information on the patient group data used to derive the SCORE2-OP model.

Name	Mean	SD	Unit
Age	73	5	Years
SBP	152	23	mmHg
Total cholesterol	6.4	1.2	mmol/L
HDL-cholesterol	1.5	0.4	mmol/L

Table 7. This table contains categorical characteristics on the patient group data used to derive the SCORE2-OP model.

Name	Number of patients
Total number of participants	28,503 (50% male)
Current smoker	20%
Type 2 Diabetes Mellitus	6%
Lipid-lowering drugs use	9%

After model derivation, the model was externally validated in a total of 338,615 individuals from 6 cohorts. Internal validation showed a good discrimination with a n C-index of 0.66 (95% CI 0.65-0.66). The external validation yielded C-indices between 0.63 (0.61-0.65) and 0.67 (0.64-0.69).

8.3.3. SCORE2-Diabetes

The SCORE2-Diabetes working group presented the SCORE2-Diabetes in their 2023 paper. It was based on the previously derived SCORE2, and the process was described in the paper al follows;

"First, the original SCORE2 risk prediction models for fatal and non-fatal CVD outcomes were adapted for use in individuals with type 2 diabetes using individual-participant data from four population data sources [Scottish Care Information—Diabetes (SCID), Clinical Practice Research Datalink (CPRD), UK Biobank (UKB), Emerging Risk Factors Collaboration (ERFC)] across seven countries (England, Wales, Scotland, France, Germany, Italy, and the USA). Model derivation involved a total of 229 460 participants with diabetes and without history of CVD at baseline from SCID, CPRD, and ERFC/ UKB."

In **Table 8** and **Table 9** information on the characteristics of patient data used to derive and validate the model is provided.

Table 8. This table contains information on the patient group data used to derive the SCORE2-Diabetes model.

Name	Mean	SD	Unit
Age	64	11	Years
SBP	137	16	mmHg
Total cholesterol	4.4	1.0	mmol/L
HDL-cholesterol	1.3	0.4	mmol/L
Age diagnosis Diabetes	58	11	per 5-years
HbA1c	56	18	mmol/mol
eGFR	76	19	mL/min/1.73 m2
Follow up	9.4	-	Years

Table 9. This table contains categorical characteristics of patient group data used to derive the SCORE2-Diabetes model.

Name	Number of patients
Male sex	229,460 (53% male)
Current smoker	38,223 (17%)
Events	43,706
Competing events	28,226

After model derivation external validation was performed on 217,036 further individuals, showing 38,603 events, from four countries.

8.4. Implementation by Evidencio

To increase the ease of use, Evidencio has integrated the three main models into single CE-certified medical device software under the name "SCORE2". All models can be accessed through a single user interface on the site and through the same model version via the API.

Depending on the input for the variables "Age" and "Type 2 Diabetes Mellitus" one of the sub-algorithms will be used to calculate the 10-year cardiovascular risk, in accordance with the clinical indications and clinical contra-indications of each individual model.

8.5. Supporting publication & Related files

Several relevant studies, such as the original derivation study by SCORE2 working group and ESC Cardiovascular risk collaboration are contained in **Table 10**. 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 10. Overview of selection of supporting publications & Related files.

Derivation studies	**SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe** *SCORE2 working group and ESC Cardiovascular risk collaboration* https://pubmed.ncbi.nlm.nih.gov/34120177/ **DOI: 10.1093/eurheartj/ehab309**
	SCORE2-OP risk prediction algorithms: estimating incident cardiovascular event risk in older persons in four geographical risk regions *SCORE2-OP working group and ESC Cardiovascular risk collaboration* https://pubmed.ncbi.nlm.nih.gov/34120185/ **DOI: 10.1093/eurheartj/ehab312**
	SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe *SCORE2-Diabetes Working Group and the ESC Cardiovascular Risk Collaboration* https://pubmed.ncbi.nlm.nih.gov/37247330/ **DOI: 10.1093/eurheartj/ehad260**

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 SCORE2: https://www.evidencio.com/models/show/2570, 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. Please make sure the correct model version is selected.

9. Implementation of the model through an API

The SCORE2 can be used through Evidencio's API to allow for (automated) calculation of the 10-year fatal & non-fatal cardiovascular disease risk. 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.

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.

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 developed to work on the latest versions, as of the making of this manual, of the four most commonly used internet browsers; Google Chrome, Mozilla Firefox, Microsoft Edge, and Apple Safari.

The tool can also be accessed on mobile devices running the most recent versions of the Android and iOS operating systems.

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 1**. The model landing page contains the following sections, that are indicated in **Figure 1**.

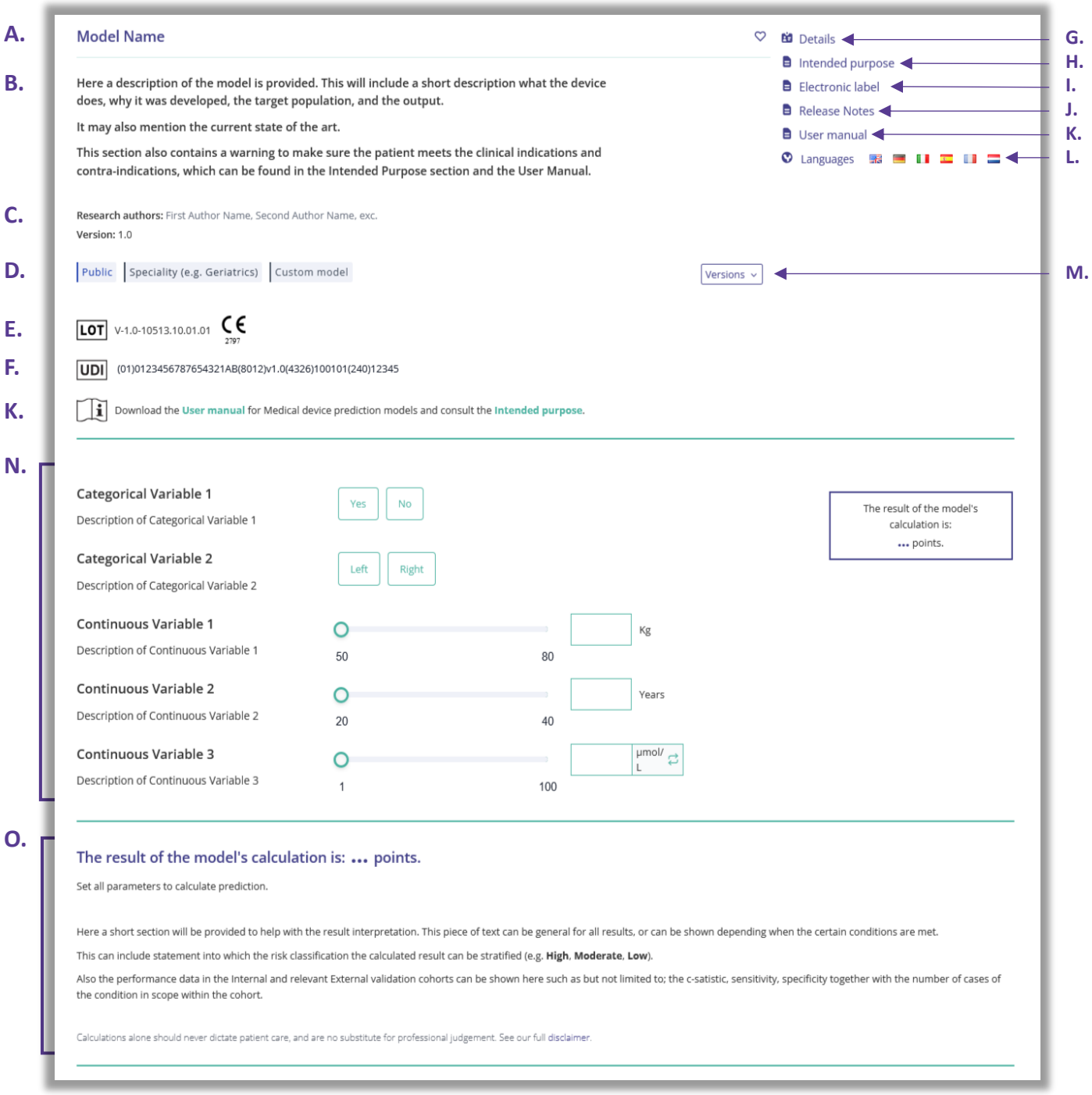

Figure 1. Example of a model landing page on the Evidencio website.

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 information on the UDI-PI Number see **Section 5.2** on **page 5** of this user 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 in **Figure 2**. 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.

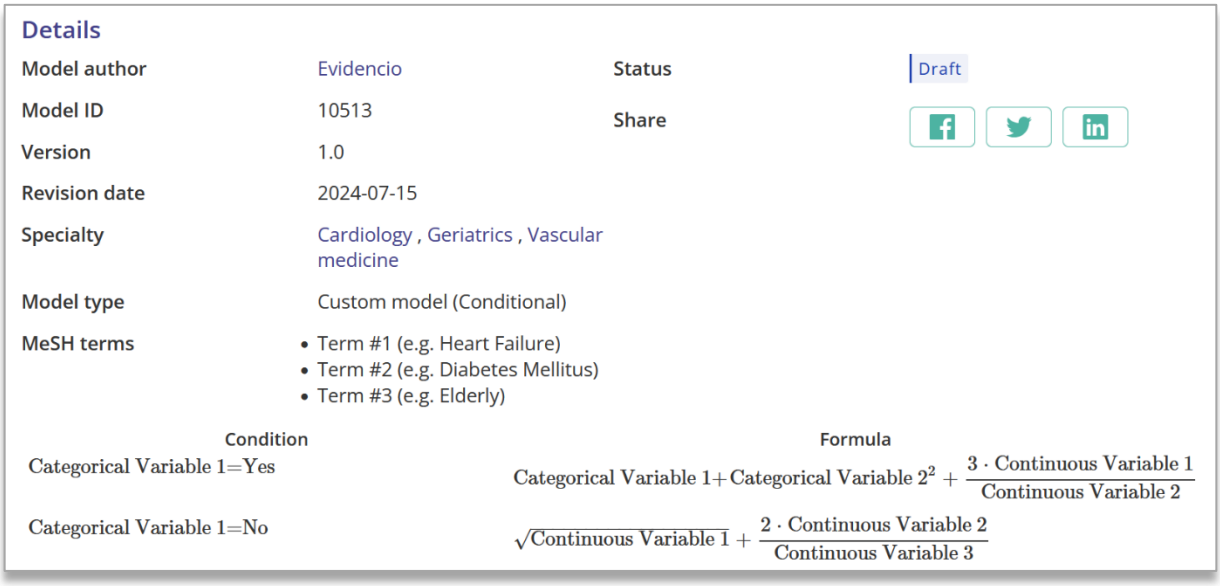

Figure 2. Example of first part of detail section.

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 3**.

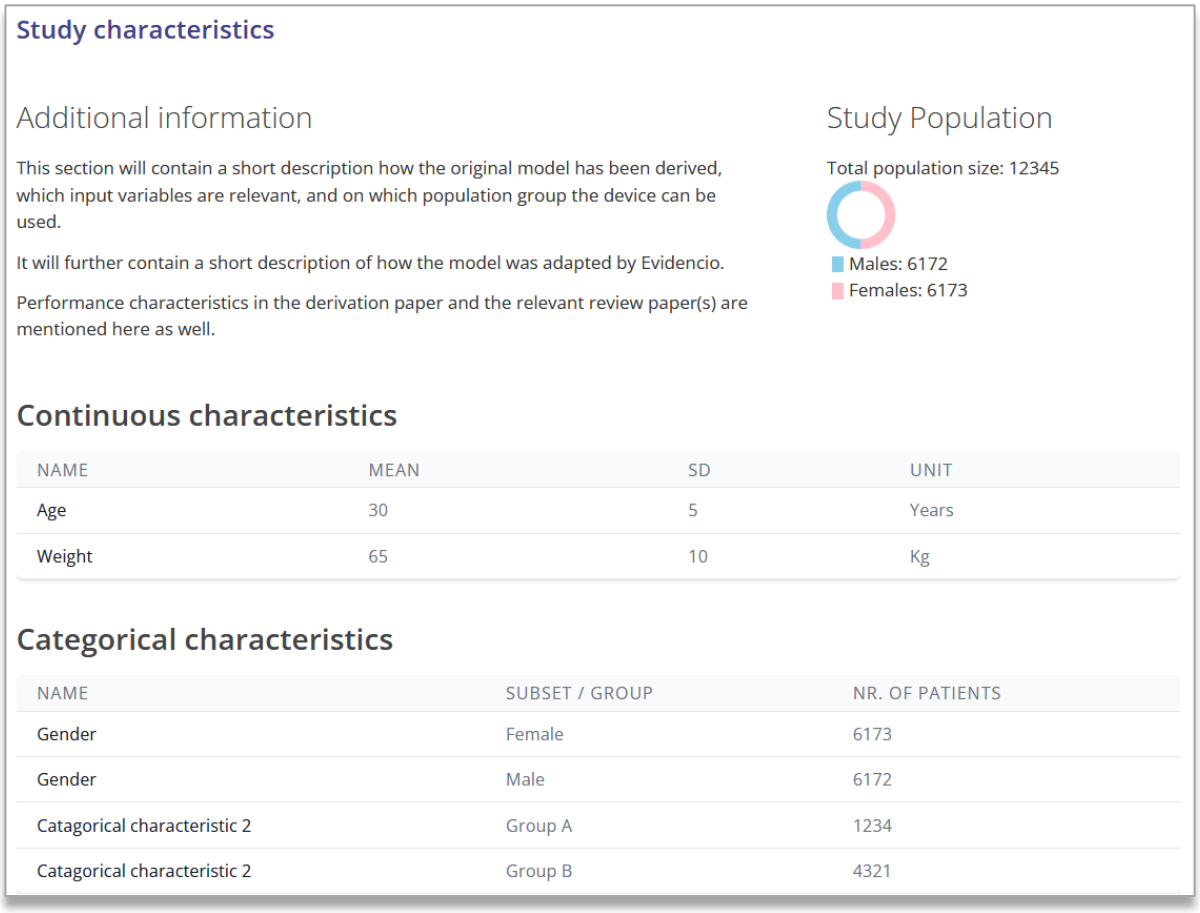

Figure 3. Example of the study characteristics section under the Details tab.

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 4**.

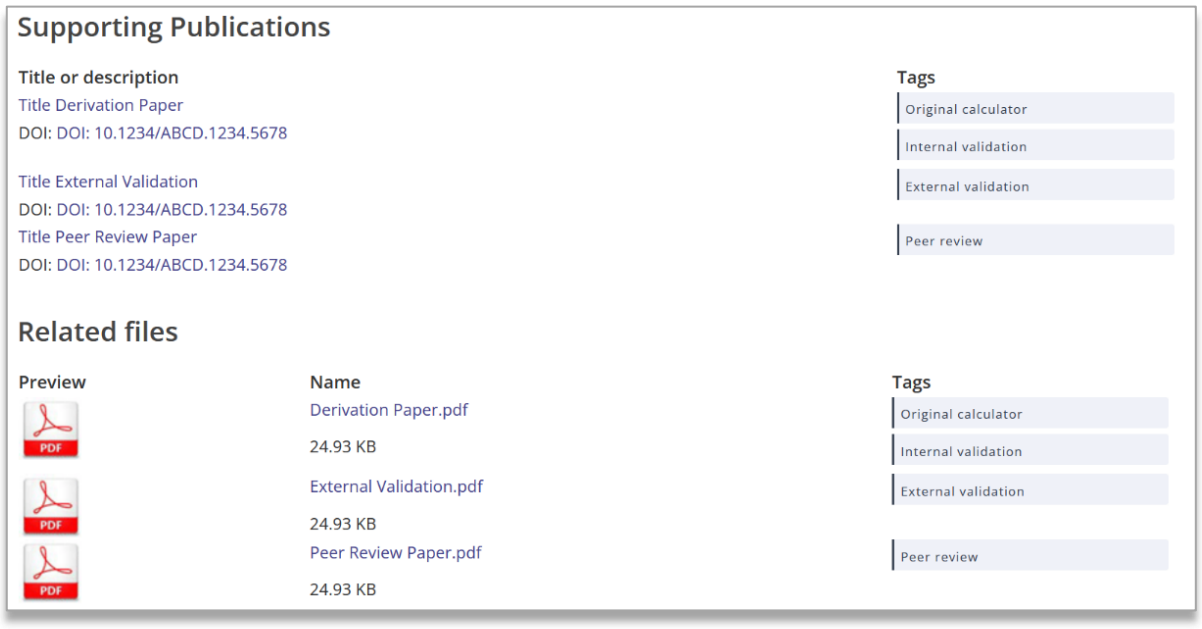

Figure 4. Example of the Supporting publication & Related files section under the Details tab.

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 6**.

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 5**.

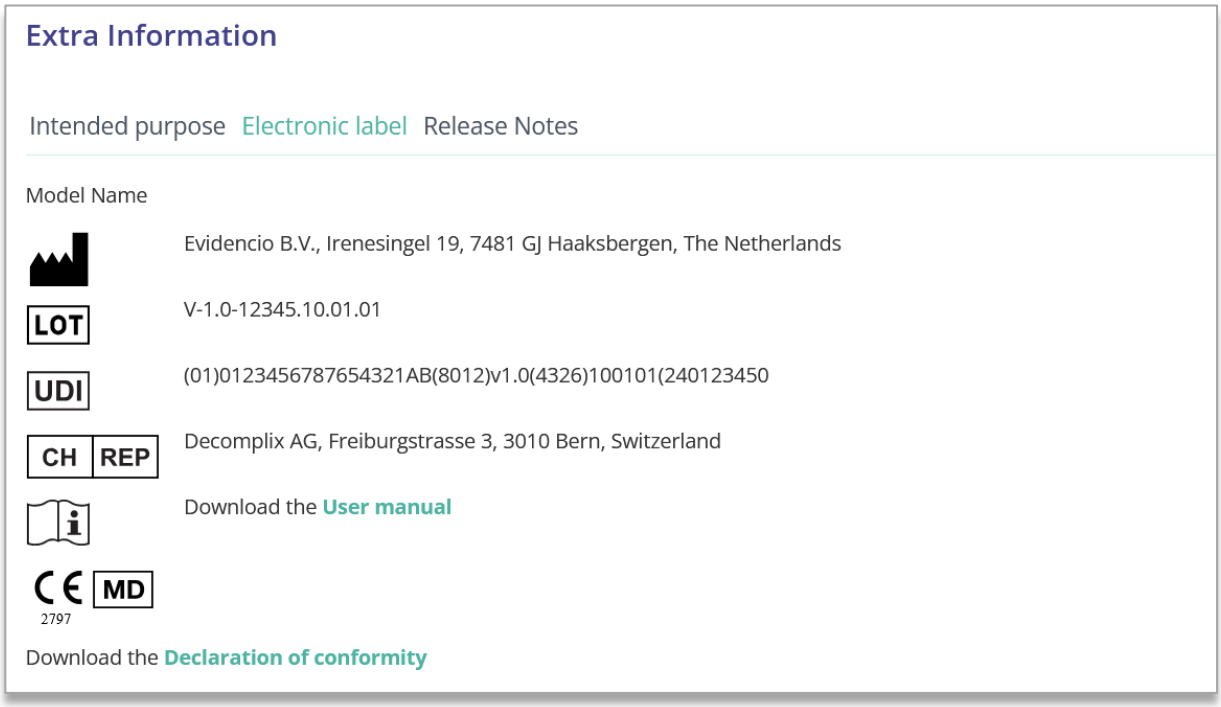

Figure 5. Example of an electronic label under the Electronic Label tab.

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 6**. The user manual page is shown in **Figure 7**. 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.

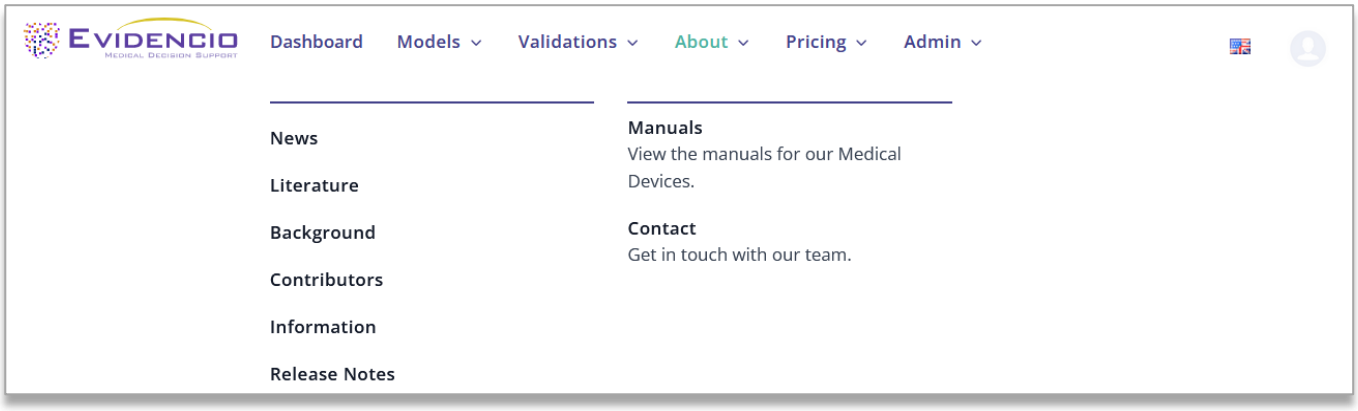

Figure 6. The drop-down menu where the user manual page can be found.

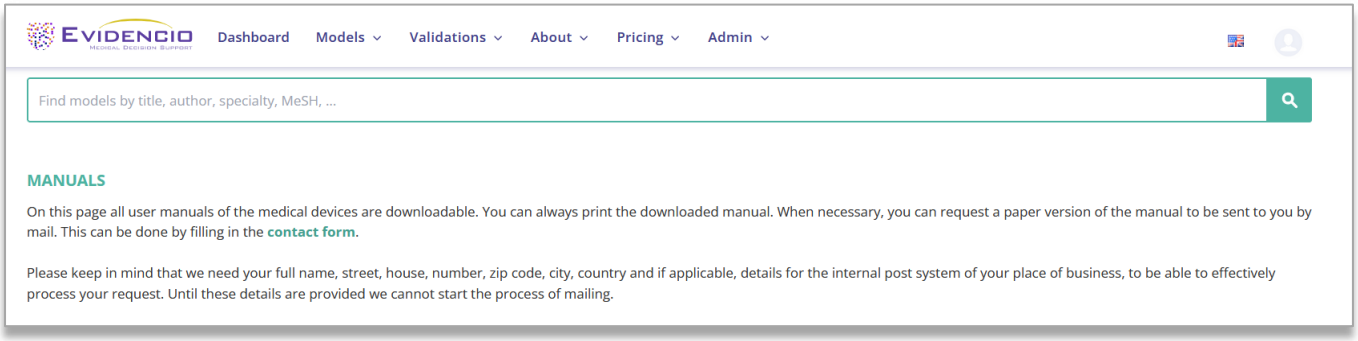

Figure 7. The user manual page for all user manuals.

L. Languages

Here an overview of languages in which the SCORE2 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. When other languages are available, these can be selected here.

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, 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. Version selection

If available, clicking on the Version tab allows the user to select a different version of the SCORE2 for a list as displayed in **Figure 8**. Please note that the model currently selected is not presented in the dropdown menu.

Figure 8. 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 shown in **Figure 9** and **Figure 10**, 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 10**.

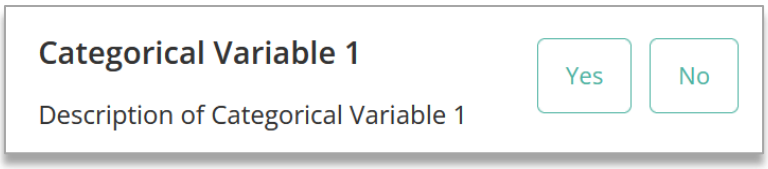

Figure 9. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.

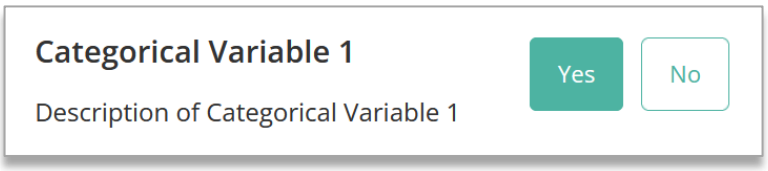

Figure 10. Example of a categorical variable, where the "Yes" button has been clicked.

Continuous variables

In the example shown in **Figure 11**, 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**).

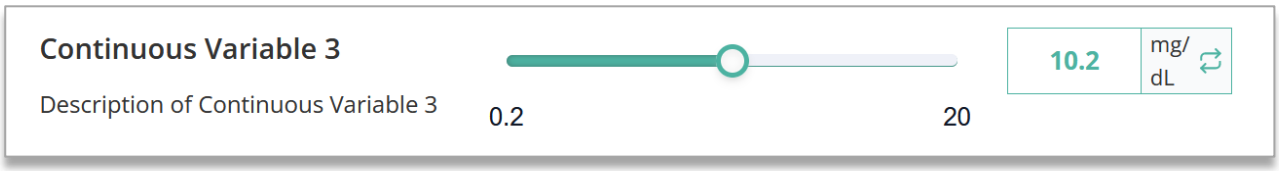

Figure 11. Example of a continuous variable, where "10.2 mg/dL" has been entered.

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See **Figure 12** below where the unit has been clicked and switched.

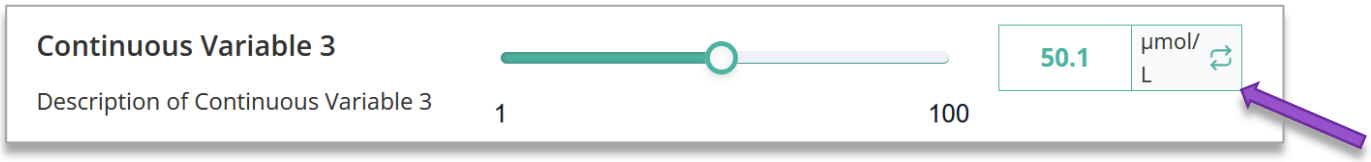

Figure 12. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

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 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 13**.

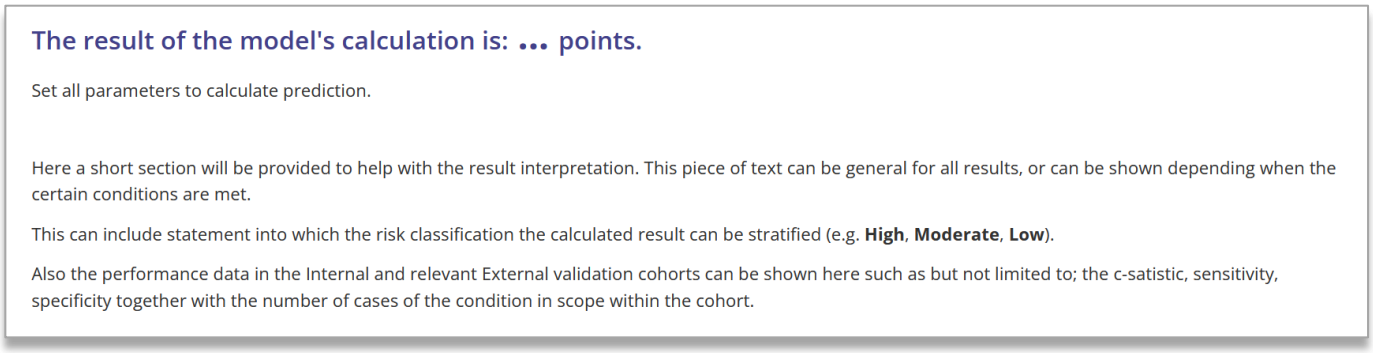

Figure 13. Example of the result display and information section.

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