User manual for the MELD Score

MELD 1.0
MELD Na (UNOS/OPTN)
MELD 3.0

Version 4, July 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 MELD Score, (which covers the MELD 1.0, MELD Na (UNOS/OPTN), and MELD 3.0 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 6.4.1** and **6.4.2** 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.

No security or privacy-sensitive personal and health-related data is stored after the use of CE-certified Medical Device Software (MDSW) models provided by Evidencio. When using the online platform, any new input, the closing of the browser tab and the refreshing of the page will remove the previously provided input. Only user data regarding which devices are used when and by whom are logged.

4. Device Description MELD Score

The MELD Score can be used to estimate the 3-month mortality risk or 90-day survival probability of patients with end-stage liver disease.

The MELD Score consists of three different algorithms that largely overlap in their required input variables and presented outcomes and which can all be used independently. This singular term is used for clarity and brevity when a statement applies to all three model. Differences between the separate devices will be mentioned when applicable.

The MELD 1.0 was originally developed to predict patient survival and identify those patients whose liver-related mortality post-TIPS (Transjugular intrahepatic portosystemic shunts) would be 3 months or less. Subsequent research showed the applicability of this prediction model to a wider patient group, predicting the 3-month risk of patients with end-stage liver disease.

With the aim of improving the accuracy of these predictions, the variable Serum Sodium was supplemented and recalibrating existing equation coefficients, resulting in the MELD Na (UNOS/OPTN), mostly used in the USA.

Relatively recently in 2021, the MELD 3.0 was introduced, adding the variable of patients Sex while removing the act of regular Hemodialysis. The outcome of the MELD 3.0 is also different compared to the other models, now calculating the 90-day survival. In part due to its novelty MELD 3.0 has yet to reach the wide scale adoption and integration into clinical guidelines compared to the MELD 1.0.

5. Electronic Label

The electronic label of this device contains the following information:

Name of the device: MELD Score

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

LOT number

MELD 1.0:	V-1.2-10085.24.07.17
MELD Na (UNOS/OPTN):	V-2.0-10085.24.07.17
MELD 3.0:	V-4.0-10085.24.07.17

UDI-PI number:

MELD 1.0:	(01)08720938015212(8012)v1.2(4326)240717(240)10085
MELD Na (UNOS/OPTN):	(01)08720938015229(8012)v2.0(4326)240717(240)10085
MELD 3.0	(01)08720938015236(8012)v3.0(4326)240717(240)10085

The electronic label can be found on the Evidencio website, see also **section H** 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.

The version number, also part of the UDI-PI, is linked to one of the three sub-models. Version 1.2 for the MELD 1.0, version 2.0 for the MELD Na (UNOS/OPTN), and version 3.0 for the MELD 3.0.

6. Intended Purpose

6.1. Intended Medical Use

The MELD Score 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 3-month mortality risk or 90-day survival probability.

The MELD Score consists of three different algorithms that largely overlap in their required input variables and presented outcomes.

The MELD 1.0 combines the following inputs to predict the 3-month mortality risk.

- Bilirubin
- Creatinine
- International Normalised Ratio (INR)

The MELD Na (UNOS/OPTN) requires the same input variables as the MELD 1.0, with the addition of sodium as a risk factor input to predict the 3-month mortality risk:

- Bilirubin
- Creatinine
- International Normalised Ratio
- Sodium

The MELD 3.0 further added sex and albumin values as risk factors to predict the 90-day survival probability.

The device is intended to be used for patients with end-stage liver disease. The result of the MELD Score 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 MELD Score is not intended to replace clinical decision-making, it can only provide information to the user on the 3-month mortality risk or 90-day survival probability. The user can use this information to support clinical decision-making regarding the prognosis and treatment of the patient. In practice, this typically entails the decisions involving palliative care or liver transplantation.

6.2. Input variables

To perform the calculations successfully, the devices comprising the MELD Score requires the input of all input variables. Which input variables are part of the equation differs between the devices, an overview of which is given in **Table 1**, **Table 2**, and **Table 3**, for the MELD 1.0, MELD Na (UNOS/OPTN), and MELD 3.0 respectively**.**

Table 1. Variables used as input for the MELD 1.0. For some variables, the units can be switched.

Name	Description	Type	Range (step size)	Units
Serum Bilirubin	Values below 17.1 µmol/L (1.0 mg/dL) are set to 17.1 µmol/L (1.0 mg/dL)	Continuous	1.5 – 850 (0.1	*µmol/L*
			0.1 – 45 (0.1)	*mg/dL*
INR	International Normalized Ratio, Values below 1.0 are set to 1.0	Continuous	0.5 – 20 (0.1)	-
Serum Creatine	Values below 88.42 µmol/L (1.0 mg/dL) are set to 88.42 µmol/L (1.0 mg/dL)	Continuous	10 – 850 (1)	*µmol/L*
			0.2 – 9 (0.01)	*mg/dL*
			Input options	
Hemodialysis	Dialysis at least twice in the past week. If yes, serum creatinine will be set to 4.0	Categorical	**Yes**	**No**

Table 2. Variables used as input for the MELD Na (UNOS/OPTN). For some variables, the units can be switched.

Name	Description	Type	Range (step size)	Units
Serum Bilirubin	Values below 17.1 µmol/L (1.0 mg/dL) are set to 17.1 µmol/L (1.0 mg/dL)	Continuous	1.5 – 850 (0.1	*µmol/L*
			0.1 – 45 (0.1)	*mg/dL*
INR	International Normalized Ratio, Values below 1.0 are set to 1.0	Continuous	0.5 – 20 (0.1)	-
Serum Creatine	Values below 88.42 µmol/L (1.0 mg/dL) are set to 88.42 µmol/L (1.0 mg/dL)	Continuous	10 – 850 (1)	*µmol/L*
			0.2 – 9 (0.01)	*mg/dL*
Serum Sodium	Sodium is limited to a range of 125-137 mmol/L. If outside these bunds, is set to the nearest limit.	Continuous	100 – 150 (1)	*mmol/L*
			100 – 150 (1)	*mEq/L*
			Input options	
Hemodialysis	Dialysis at least twice in the past week. If yes, serum creatinine will be set to 4.0	Categorical	**Yes**	**No**

Table 3. Variables used as input for the MELD 3.0. For some variables, the units can be switched.

Name	Description	Type	Range (step size)	Units
Serum Bilirubin	Values below 17.1 µmol/L (1.0 mg/dL) are set to 17.1 µmol/L (1.0 mg/dL)	Continuous	1.5 – 850 (0.1	*µmol/L*
			0.1 – 45 (0.1)	*mg/dL*
INR	International Normalized Ratio, Values below 1.0 are set to 1.0	Continuous	0.5 – 20 (0.1)	-
Serum Creatine	Values below 88.42 µmol/L (1.0 mg/dL) are set to 88.42 µmol/L (1.0 mg/dL)	Continuous	10 – 850 (1)	*µmol/L*
			0.2 – 9 (0.01)	*mg/dL*
Serum Sodium	Sodium is limited to a range of 125-137 mmol/L. If outside these bunds, is set to the nearest limit.	Continuous	100- 150 (1)	*mmol/L*
			100 – 150 (1)	*mEq/L*
Serum Albumin	Limited to a range 15-35 g/L (1.5 – 3.5 g/dL). Values outside this range are set to the nearest limit.	Contiguous	*0 – 50 (1)*	*g/L*
			0 – 5 (0.1)	*g/dL*
			Input options	
Sex	Sex of the patient	Categorical	**Female**	**Male**

6.3. Clinical Benefit

Correct functioning of the MELD Score can result in these clinical benefits:

- The MELD Score can aid a professional in providing a patient with an accurate prognosis. More accurate prognosis can support necessary decision-making of patients with end-stage liver disease and organisation of their life, such as the need for palliative care.
- Use of the Meld Score can positively impact patient management by supporting the decision-making concerning application for a liver transplantation.
- Digital implementation of the algorithm underlying the MELD Score 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.

6.4. Indented target population and exclusion

The MELD Score is intended to be used only for a specific group of patients, corresponding to the below indications and contra-indications.

6.4.1. Clinical Indications

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

- Patients should be at least 18 years or older *
- Having end-stage liver disease

**The authors of the MELD Score suggest that it can be used for patients of 12 years or older. However, this is not universally accepted, e.g. the OPTN policy acknowledges three groups: less than 12 years, 12 or older and 18 or older. In contrast, Eurotransplant uses an age limit of 18 years or older, below which the PELD is recommended. Because of this lack of consensus, the age for the use of the MELD Score is set to 18 years or older*

6.4.2. Clinical contra-indications

The MELD Score is contra-indicated for patients with certain medical conditions, known as 'MELD Exceptions'. Several liver allocation and transplantation programs provide additional points to patients with these conditions to compensate for them for the purpose of equity among patients regarding liver allocation. This measure is due to the fact that the MELD Score results are considered to not accurately represent the mortality risk of patients with these conditions. However, there

is no consensus on the exact list of conditions that should be regarded as exceptions as well as how to deal with them (e.g. the number of points to be distributed) to reach equity for all patients.

The following conditions are acknowledged as MELD Exceptions in different liver allocation and transplantation programs, and thus the use of the MELD Score for patients with these conditions should be performed with caution and the MELD Score results should be interpreted within the context of the condition:

Generally acknowledged MELD Exceptions:

- Hepatopulmonary syndrome (HPS)
- Portopulmonary hypertension (PPH)
- Primary hyperoxaluria
- Cystic fibrosis (CF)
- Cholangiocarcinoma (CCA)
- Hepatocellular carcinoma (HCC) (often together with Milan criteria to determine if HCC patients are eligible/suitable for transplantation)

Additionally, the ELITA acknowledges the following exceptions:

- Cholangitis (Primary sclerosing cholangitis and biliary sepsis/secondary sclerosing cholangitis)
- Neuroendocrine tumours
- Polycystic liver disease (PLD)Hepatic artery thrombosis (HAT)
- Persistent hepatic dysfunction (incl. small-for-size syndrome)
- Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber-Syndrome)
- Biliary atresia
- Non-metastatic hepatoblastoma
- Urea-cycle disorder/organic acidemia
- Hepatic hemangioendothelioma

Moreover, the following exceptions are mentioned in other literature:

- Familial amyloid polyneuropathy (FAP)
- (Unusual) metabolic disease
- Hepatorenal syndrome (HRS) (Eurotransplant region)
- Amyloidosis

Acknowledged by the 2006 MELD Exception Study Group and Conference (MESSAGE):

- Unusual tumour
- Unusual metabolic disease
- Ascites
- Hepatic encephalopathy
- Gastrointestinal bleeding
- Budd-Chiari Syndrome (BCS)
- Pruritus

Moreover, in an OPTN proposal for addition of serum sodium, it is stated that the serum sodium values for patients with hyperglycemia should be corrected via an additional formula. Thus, caution is also necessary if the MELD Score is used for these patients.

6.5. Lifetime, residual risks and side effects

The MELD Score 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.

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

The MELD Score is a low-risk device, there are no noticeable risks involved outside of possible mis-estimation of a patient's 3-month or 90–day mortality risk, 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 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 MELD Score does not have any direct side effects relevant for the patient.

6.6. User profile

The MELD Score 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

6.7. 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.

6.8. 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.

6.9. Versions of the MDSW

The version of the MELD Score concerns the initial version of MDSW of which Evidencio is the manufacturer.

6.10. Functioning, physical principle

The MDSW's underlying mathematical formula concerns a combination of a risk score model and a Cox regression model. The risk score model results in a specific number of points that correspond to a mortality risk. The acquisition and processing of the data, the analyses to assemble the relevant criteria for the MDSW as well as the setup and refinement of the MELD Score are provided in the instructions for use. Entering the details for an individual in the MDSW initiates the estimation of short-term mortality risk.

7. Result interpretation

The MELD 1.0 and MELD Na (UNOS-OPTN) provide the same 2 output statements;

- **MELD score**

This score is the outcome the formula for which the patients' values are the input combined with derived the derived coefficient rounded to the nearest whole integer.

- **MELD (estimate 3-month mortality)**

Form this MELD score a mortality risk is determined. The MELD 1.0 and MELD Na (UNOS/OPTN) link certain ranges of the MELD scores to specific risk percentages.

Different from the MELD 1.0 and MELD Na (UNOS/OPTN), the MELD 3.0 provide beside a MELD score the

- **MELD (estimated 90-day survival)**

This risk, given in percentages, is equated from the calculated MELD score using a single formula. This allows for a more precise and continuous relationship between the MELD score and change for survival.

The MELD Score is not intended to replace clinical decision-making, it can only provide information to the user on the 3-monthmortality risk. The user can use this information to support clinical decision-making regarding the prognosis and treatment of the patient.

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	T. Pasman	
Model ID	10085	
	Version number	**Revision date**
MELD 1.0	1.2	17 July 2024
MELD Na (UNOS/OPTN)	2.0	17 July 2024
MELD 3.0	3.0	17 July 2024
Speciality	Hepatology	
Model type	R-Script model	
MeSH terms	• Risk • Hepatology • Creatinine • Sodium • INR	• Bilirubin • End Stage Liver Disease • Mortality • Liver • Dialysis

8.2. Study characteristics

The performance of the MELD 1.0, MELD Na (UNOS/OPTN), and MELD 3.0 of the MELD score were assessed with data from at least 269,942, 340,378, and 41,083 different patients respectively.

In terms of discrimination, the MELD 1.0, MELD Na (UNOS/OPTN), and MELD 3.0 performed well. Their discriminatory performance was similar to each other. The C-statistics of the MELD 1.0, the MELD Na (UNOS/OPTN), and MELD 3.0 were 0.80 (95% CI: 0.74 – 0.85). 0.78 (95% CI: 0.63 – 0.89), and 0.79 (95% CI: 0.62 – 0.90) respectively.

8.3. Supporting publication & Related files

The equation used by the MELD 1.0 was derived in a paper by Malinchoc *et al*. (2000) and later refined by Kamath *et al*. (2001). This was followed by an update on the interpretation of the outcome by Wiesner *et al*. (2003), which is adopted in most guidelines as well as by Evidencio.

For the MELD Na (UNOS/OPTN) an adjusted version which added Serum Sodium levels to the variables was developed by Biggins *at al*. (2006), and was proposed to be adopted by the United Network for Organ Sharing (UNOS), and the Organ Procurement & Transplantation Network (OPTN) in the US in 2014 and 2013 respectively.

The development of the MELD 3.0 was described by Kim *et al*. (2021), who aimed to optimize the MELD 1.0 further by integrating additional variables (Sex and Serum Albumin), removing Hemodialysis as and variable, and updating the coefficients of existing variables.

The most relevant studies are contained in **Table 4**. 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 4. Overview of selection of supporting publications & Related files.

Development paper MELD 1.0	**A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts** (2000) *M Malinchoc , P S Kamath, F D Gordon, C J Peine, J Rank, P C ter Borg* DOI: 10.1053/he.2000.5852
Development paper MELD 1.0	**A model to predict survival in patients with end-stage liver disease** (2001) *P S Kamath, R H Wiesner, M Malinchoc, W Kremers, T M Therneau, C L Kosberg, G D'Amico, E R Dickson, W R Kim* DOI: 10.1053/jhep.2001.22172
Development paper MELD 1.0	**Model for end-stage liver disease (MELD) and allocation of donor livers** (2003) *Russell Wiesner, Erick Edwards, Richard Freeman, Ann Harper, Ray Kim, Patrick Kamath, Walter Kremers, John Lake, Todd Howard, Robert M Merion, Robert A Wolfe, Ruud Krom* DOI: 10.1053/gast.2003.50016
Development paper MELD Na (UNOS/OPTN)	**Evidence-based incorporation of serium sodium concentration into MELD** (2006) *Scott W Biggins, W Ray Kim, Norah A Terrault, Sammy Saab, Vijay Balan, Thomas Schiano, Joanne Benson, Terry Therneau, Walter Kremers, Russell Wiesner, Patrick Kamath, Goran Klintmalm* DOI: 10.1053/j.gastro.2006.02.010
Guidelines recommending MELD Na (UNOS/OPTN) for the USA.	**Proposal to add Serum Sodium to the MELD Score** (2013) *Organ Procurement & Transplantation Network (OPTN), USA*
	Changes to OPTN bylaws and policies form June 2014 board meeting (2014) *United Network for Organ Sharing (UNOS), USA*
Development paper MELD 3.0	**MELD 3.0: The Model for End-stage Liver Disease Updated for the Modern Era** (2021) *W. Ray Kim, Ajitha Mannalithara, Julie K. Heimbach, Patrick S. Kamath, Sumeet K. Asrani, Scott W. Biggins, Nicholas L. Wood, Sommer E. Gentry, Allison J. Kwong* DOI: 10.1053/j.gastro.2021.08.050

8.4. Release notes

The release notes for each publicly available version of the device can be found on the Evidencio website page by going to the MELD Score: https://www.evidencio.com/models/show/10085, 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 MELD Score can be used through Evidencio's API to allow for (automated) estimation of the 3-month mortality risk or 90-day survival probability of patients with end-stage liver disease. 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 1**. The model landing page contains the following sections, that are indicated in **Figure 1**.

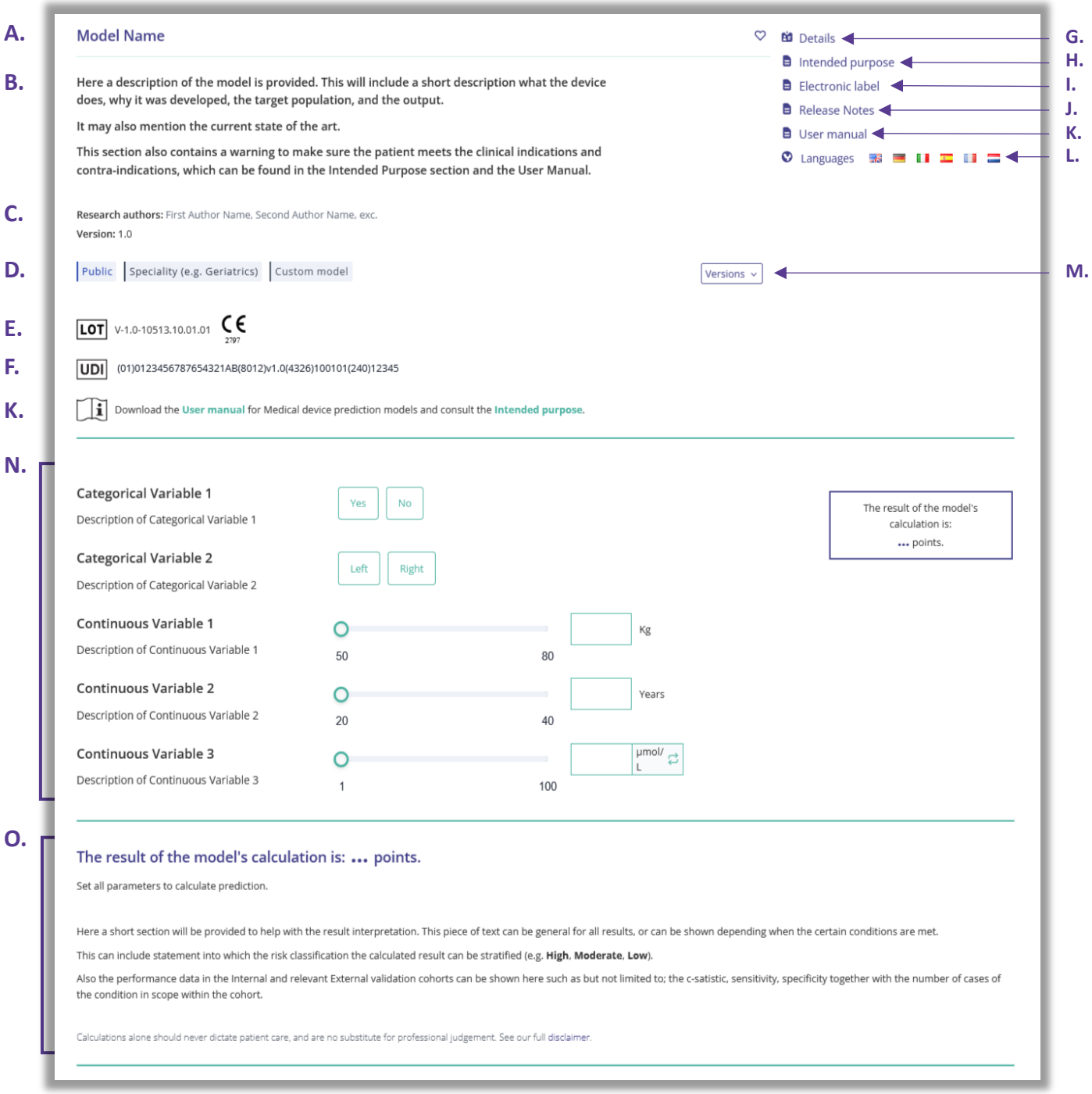


Figure 1. Example of a model landing page on the Evidencio website.

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 a description of the UDI-PI number; see **section 5.2** on **page 4** 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 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.

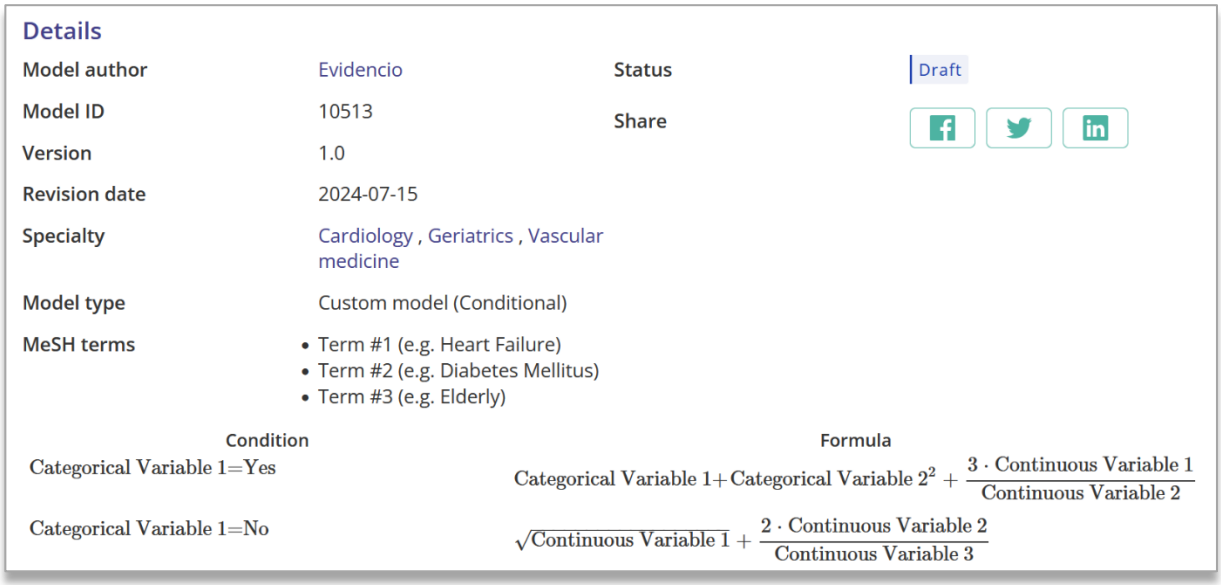
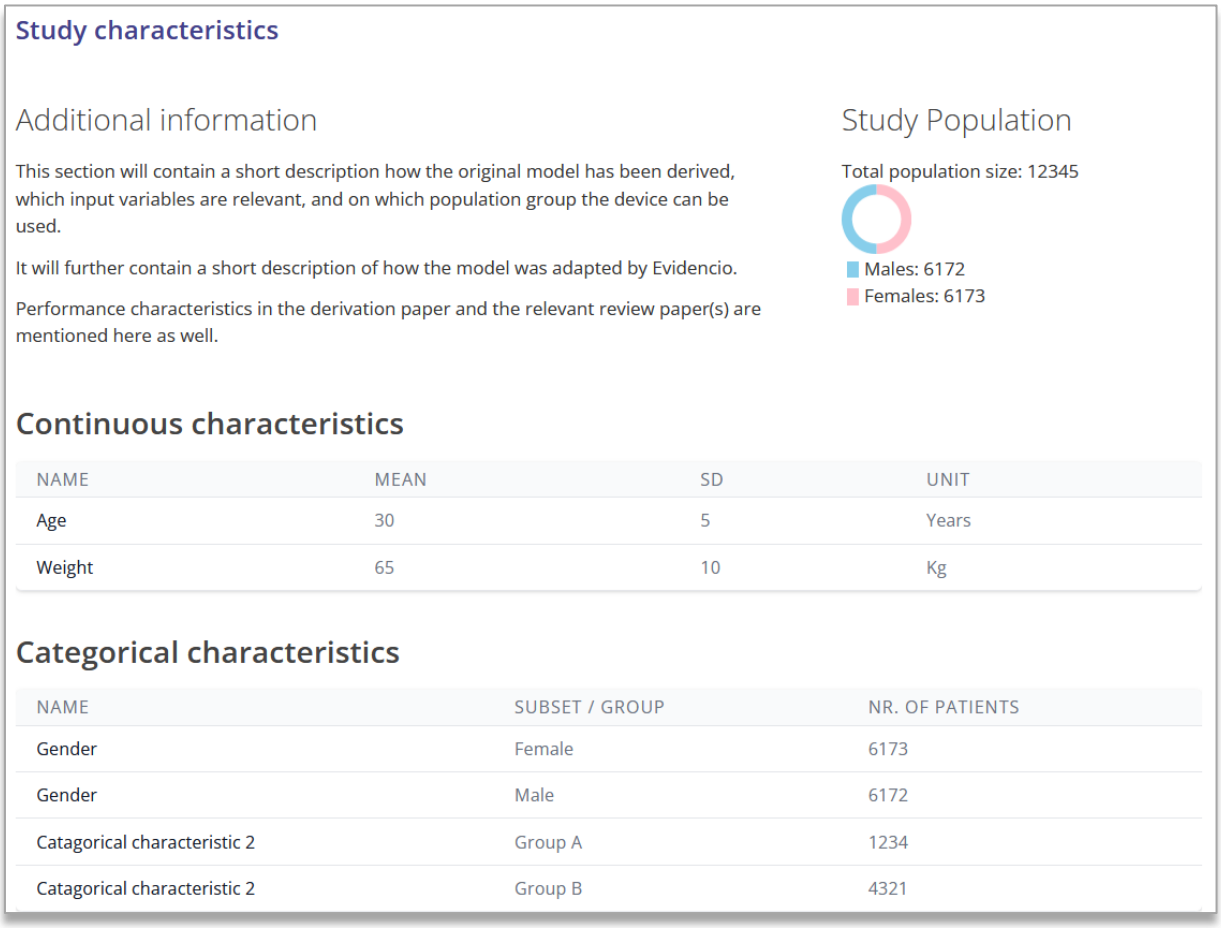


Figure 2. Example of first part of detail section.

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**



Study characteristics

Additional information

This section will contain a short description how the original model has been derived, which input variables are relevant, and on which population group the device can be used.

It will further contain a short description of how the model was adapted by Evidencio.

Performance characteristics in the derivation paper and the relevant review paper(s) are mentioned here as well.

Study Population

Total population size: 12345

Males: 6172
Females: 6173

Continuous characteristics

NAME	MEAN	SD	UNIT
Age	30	5	Years
Weight	65	10	Kg

Categorical characteristics

NAME	SUBSET / GROUP	NR. OF PATIENTS
Gender	Female	6173
Gender	Male	6172
Catagorical characteristic 2	Group A	1234
Catagorical characteristic 2	Group B	4321

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**. 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.

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

H. 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**. The electronic label is unique for each model comprising the MELD Score.

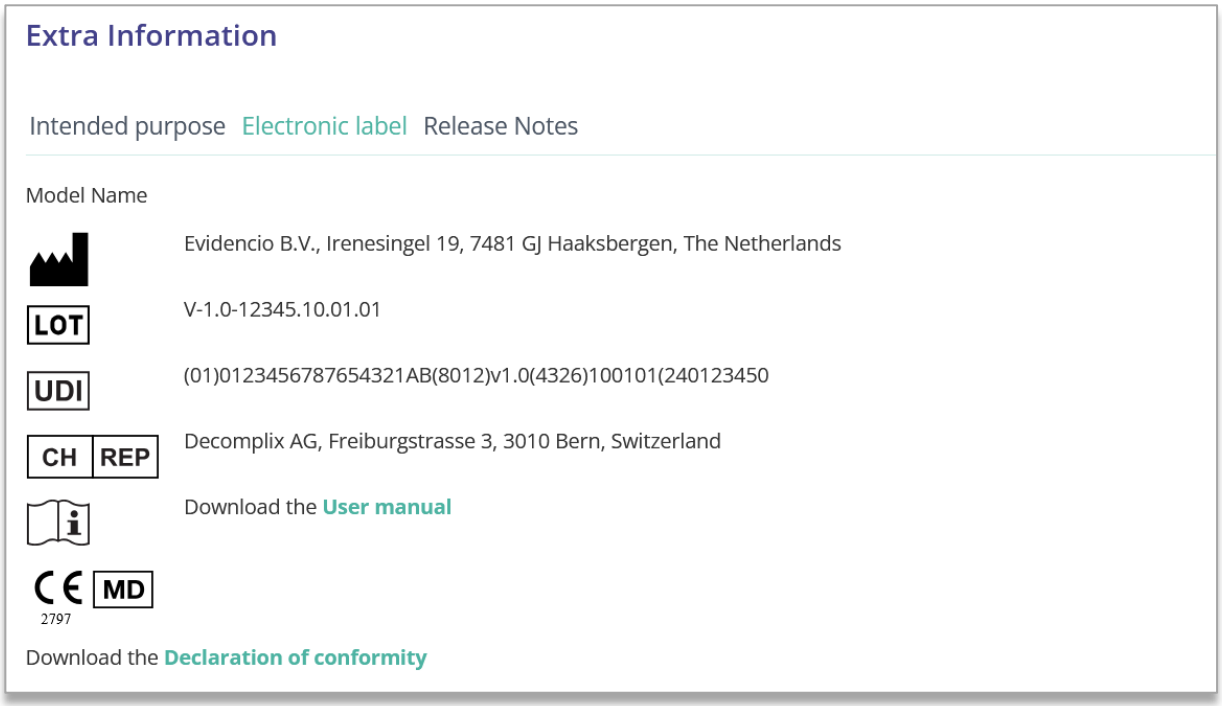


Figure 5. Example of an electronic label under the Electronic Label tab.

I. 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 4**.

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 **11** of this user manual.

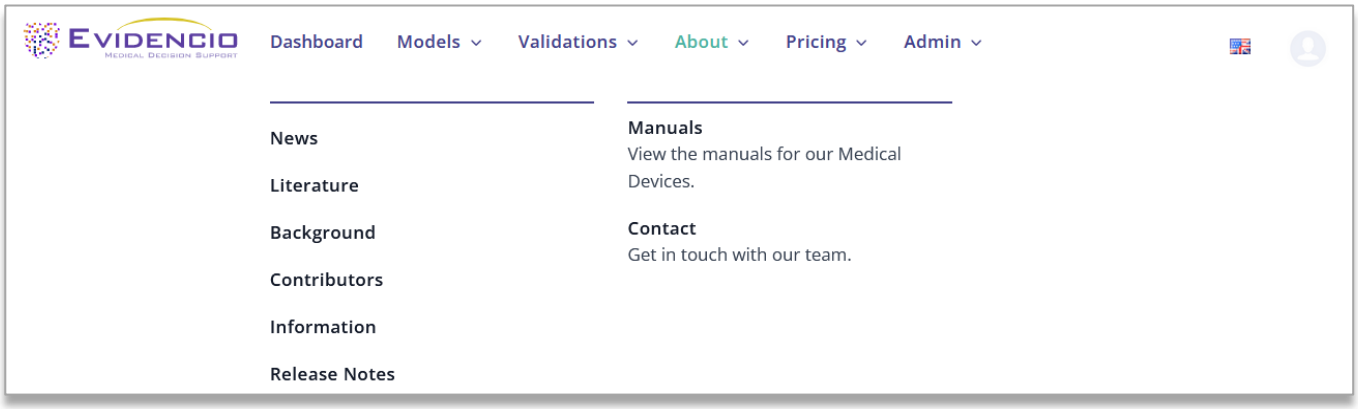


Figure 6. The drop-down menu where the user manual page can be found.

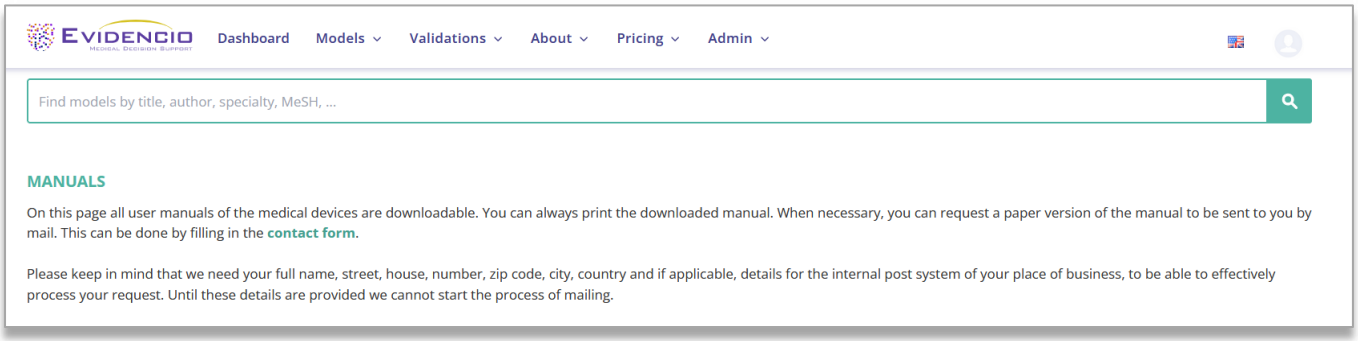


Figure 7. The user manual page for all user manuals.

L. Languages

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 MELD Score and its user manual are available in German, French, Spanish, Italian, Dutch, and 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. 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 8** and **Figure 9**, 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 9**.

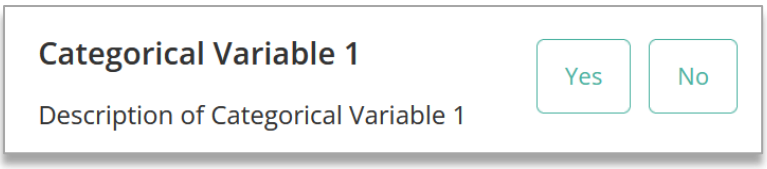


Figure 8. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.

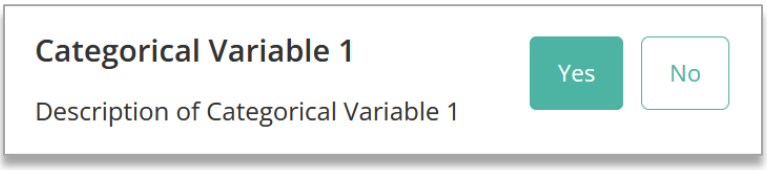


Figure 9. Example of a categorical variable, where the "Yes" button has been clicked.

Continuous variables

In the example shown in **Figure 10**, 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**).

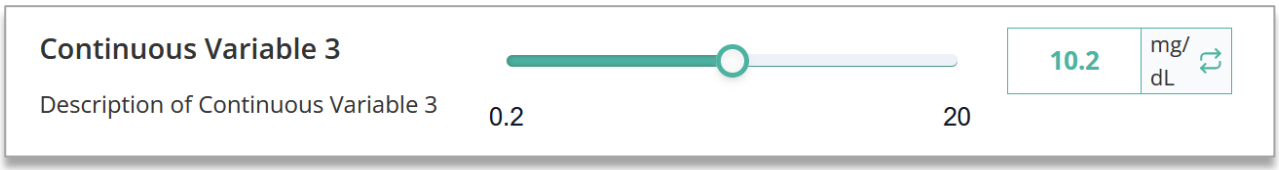


Figure 10. Example of a continuous variable, where "10.2 mg/dL" has been entered.

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See **Figure 11** below where the unit has been clicked and switched.

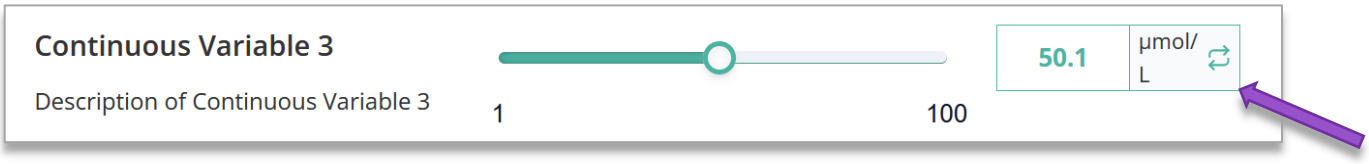


Figure 11. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

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.

N. 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 risk 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 risk stratification is provided based on the risk score. 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 12**.

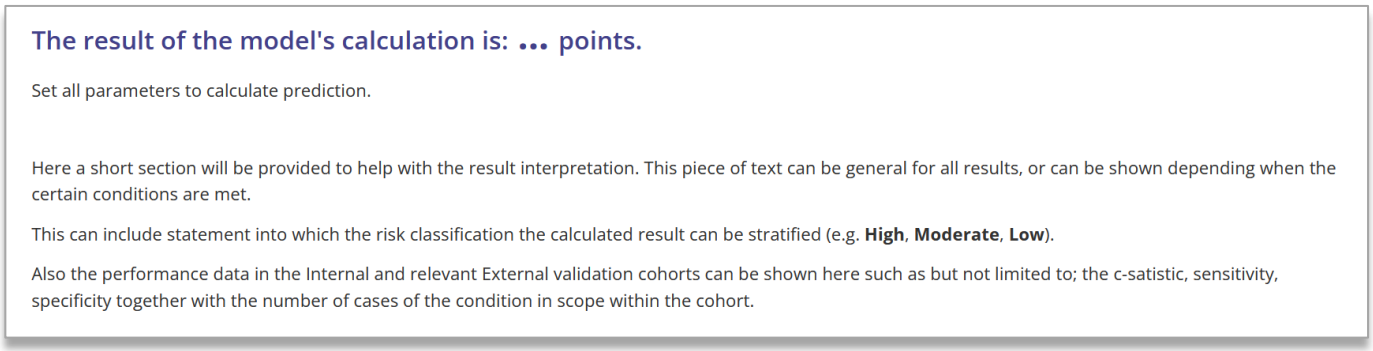


Figure 12. Example of the result display and information section.

O. Model & Version selection

Clicking on the Version tab allows the user to select the different model and version of the MELD Score for a list as displayed in **Figure 13**. Please note that the model currently selected is not presented in the dropdown menu.

Figure 13. Example of the model selection tab.

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:

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e-mail: info@evidencio.com