

File information:

Name: 2326-DOC-43 rev2.0 User manual SaMD - ABC Bleeding Risk Score Calculator.pdf
Size: 688813
Hash: EBC373CCEFDE75E5B52F9A9F561C90BA175D9D33AB2417618C56F60B99E0E100
Pages: 10

Signatories:

Role: author
Name: D.S. (Ditte) Moejes (id: 6)
Time: 2022-07-27 09:45:56 (762234)
ip: 192.168.1.50

```
ad          d0
5483        4e6c
c41c46babe1f46970d0b
2bc39f02dd1ebf22769e
c0b4 71e4c85334 719d
b28466b8d034a22bcfde
e606b24dc705d0ae
276c3c cc311f
1da15e3
48d
```

Role: reviewer
Name: E.M. (Emma) Knijn (id: 5)
Time: 2022-07-27 09:53:06 (323953)
ip: 192.168.1.49

```
a6          30
cdc7        ee4f
a4e8b4c89c3549f52022
1ed7b0038cdf3e66d90a
2d73 6acb7d76bf 1c61
10745ee030cb772b86a2
012b9d971c2c55b3
c76b9b 8e4fa2
fb94035
321
```

Role: approver
Name: R.J. (Rob) Mentink (id: 2)
Time: 2022-07-27 09:54:20 (883237)
ip: 192.168.1.37

```
4e          85
eb5e        70f3
1157a60980bd3b6a6b51
4d71b4d207976ea87cd8
9b83 3e8be3945a 72f8
0d93b7481cda0ad61cd6
f9d9ba62eabc522a
b858f5 501c79
0eeee07
c0b
```



User manual
for
The ABC Bleeding Risk Score Calculator

Version 1, 27th of July, 2022, in English

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 ABC Bleeding Risk Score Calculator. 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 here:

<https://www.evidencio.com/disclaimer>

3. Warnings



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.

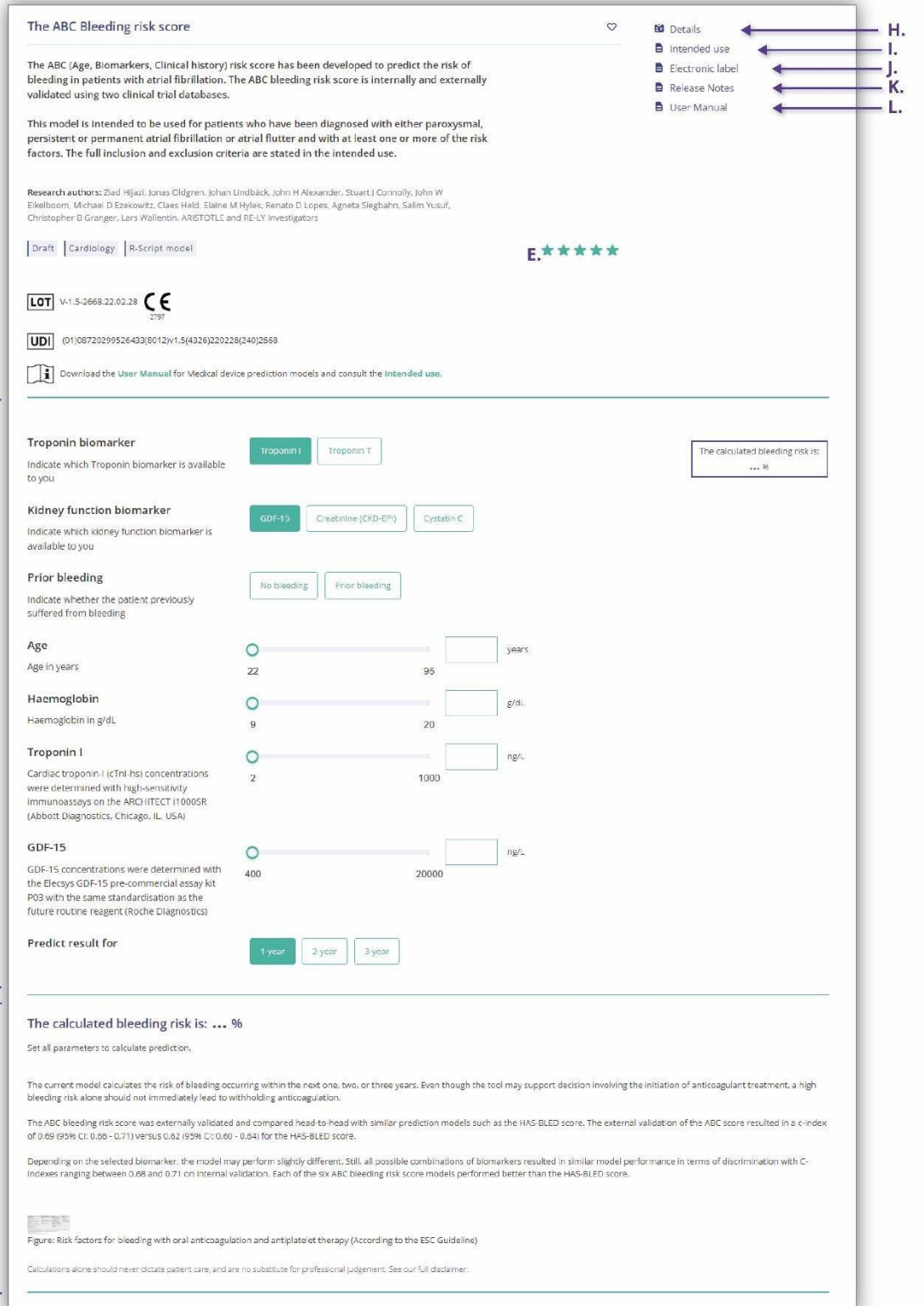
Before reading the result, double check the filled in values to prevent errors.

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.

This model is only intended for use in settings where the usage and result of a model are never urgently needed.

4. 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.



A. The ABC Bleeding risk score

B. The ABC (Age, Biomarkers, Clinical history) risk score has been developed to predict the risk of bleeding in patients with atrial fibrillation. The ABC bleeding risk score is internally and externally validated using two clinical trial databases.

This model is intended to be used for patients who have been diagnosed with either paroxysmal, persistent or permanent atrial fibrillation or atrial flutter and with at least one or more of the risk factors. The full inclusion and exclusion criteria are stated in the intended use.

C. Research authors: Ziad Hjjazi, Jonas Oldgren, Johan Lindback, John H Alexander, Stuart J Connolly, John W Eikelboom, Michael D Ezekowitz, Claes Haid, Elaine M Hylek, Renato D Lopes, Agneta Siegbahn, Salim Yusuf, Christopher D Granger, Lars Wallentin. ARISTOTLE and RE-LY Investigators

D. Draft | Cardiology | R-Script model

E. ★★★★★

F. LOT V-1.5-2668.22.02.28 2797

G. UDI (01)08720299526403(0012)1.5(4026)220228(240)2668

L. Download the User Manual for Medical device prediction models and consult the Intended use.

M.

Troponin biomarker
Indicate which Troponin biomarker is available to you
Troponin I | Troponin T

Kidney function biomarker
Indicate which kidney function biomarker is available to you
GDF-15 | Creatinine (CKD-EPI) | Cystatin C

Prior bleeding
Indicate whether the patient previously suffered from bleeding
No bleeding | Prior bleeding

Age
Age in years: 22 to 95

Haemoglobin
Haemoglobin in g/dL: 9 to 20

Troponin I
Cardiac troponin I (cTnI) hsi concentrations were determined with high-sensitivity immunoassays on the ARCHITECT II 0005R (Abbott Diagnostics, Chicago, IL, USA)
2 to 1000 ng/L

GDF-15
GDF-15 concentrations were determined with the Elecsys GDF-15 pre-commercial assay kit P03 with the same standardisation as the future routine reagent (Roche Diagnostics)
400 to 20000 ng/L

Predict result for
1 year | 2 year | 3 year

N. The calculated bleeding risk is: ... %
Set all parameters to calculate prediction.

The current model calculates the risk of bleeding occurring within the next one, two, or three years. Even though the tool may support decision involving the initiation of anticoagulant treatment, a high bleeding risk alone should not immediately lead to withholding anticoagulation.

The ABC bleeding risk score was externally validated and compared head-to-head with similar prediction models such as the HAS-BLED score. The external validation of the ABC score resulted in a c-index of 0.69 (95% CI: 0.60 - 0.71) versus 0.62 (95% CI: 0.60 - 0.64) for the HAS-BLED score.

Depending on the selected biomarker, the model may perform slightly different. Still, all possible combinations of biomarkers resulted in similar model performance in terms of discrimination with C-Indexes ranging between 0.68 and 0.71 on internal validation. Each of the six ABC bleeding risk score models performed better than the HAS-BLED score.

Figure: Risk factors for bleeding with oral anticoagulation and antiplatelet therapy (According to the ESC Guideline)

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer.

H. Details

I. Intended use

J. Electronic label

K. Release Notes

L. User Manual

Figure 1. An example of a model landing page.

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. Model rating

Evidencio can award up to 5 stars to each model, these stars are awarded when:

1. All model details are provided;
2. A TRIPOD form is added to the supporting publications;
3. An internal review is added to the supporting publications;
4. An external review is added to the supporting publications; and
5. A peer review is added to the supporting publications.

Under the "Details button", indicated by H, details are given to which of these stars are awarded for which reason. The ABC Bleeding Risk Score Calculator has 5 stars.

F. 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.

G. UDI number

The UDI number is an international tool that helps users identify and find information on products. UDI stands for Unique Device Identifier. Evidencio's UDIs have the following format:

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

The UDI-DI 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>

H. 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.

Additional information on the rating of a model can be found by hovering over the ‘i’ icon, next to the stars.

Details

Model author	T. A. Hueting	Rating	★ ★ ★ ★ ★ ⓘ
Model ID	2326	Status	Private
Version	2.1	Share	f 🐦 in
Revision date	2021-06-28		
Specialty	Cardiology		
Model type	R-Script model <small>(Calculation)</small>		
MeSH terms	<ul style="list-style-type: none"> Bleeding Atrial Fibrillation 		

Figure 2. The model details.

Study characteristics

Below the ‘Details section’ the section labeled ‘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 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 3.

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.

These tags are considered important, because the availability of particular information covered by the above mentioned tasks provide insight into the quality of the model development process and the model itself. As a completeness of information and quality indicator a model receives a certain number of stars when these labels can be assigned to relevant files or references.

Supporting Publications

Title or description

The novel biomarker-based ABC (age, biomarkers, clinical history)-bleeding risk score for patients with atrial fibrillation: a derivation and validation study
DOI: 10.1016/S0140-6736(16)00741-8

Evaluation of the Age, Biomarkers, and Clinical History-Bleeding Risk Score in Patients With Atrial Fibrillation With Combined Aspirin and Anticoagulation Therapy Enrolled in the ARISTOTLE and RE-LY Trials
DOI: 10.1001/jamanetworkopen.2020.15943

Performance of the ABC Scores for Assessing the Risk of Stroke or Systemic Embolism and Bleeding in Patients With Atrial Fibrillation in ENGAGE AF-TIMI 48
DOI: 10.1161/CIRCULATIONAHA.118.038312

ESC Clinical Practice Guidelines (2020 Guidelines for Management of Atrial Fibrillation)

Tags

- Paper
- Peer review
- Internal validation
- External validation
- Tripod
- Paper
- Peer review
- External validation
- External validation
- Paper
- Information on topic

Related files

Preview



Name

Bleeding risk factors.png
338.73 kB

Tags

- Figure (results-page)

Figure 3. An example of Supporting publications & related files. Below a list of supporting publications, a related file is added. In this case; a table with bleeding risk factors.

I. Intended use button

The intended use and (medical) purpose of the model can be found under the button: 'Intended use'. Among other things, the intended use indicates inclusion criteria of the medical device. Furthermore, the intended use comments on the appropriate use of the model regarding the intended use environment, intended users, and intended patient population (in- and exclusion criteria). For the ABC Bleeding Risk Score the following intended use is described:

Intended use

The ABC Bleeding Risk Score calculator is intended to support clinical decision making by informing clinical management on the estimated risk that an individual patient diagnosed with atrial fibrillation or atrial flutter may suffer a major bleeding within a one-year, two-year, or three-year period.

The calculator combines patient data (age) with clinical data (prior bleeding) and lab results (Troponin I, Troponin T, GDF-15, CKD-EPI, Cystatin C, and Haemoglobin) to calculate the estimated risks.

The calculator is intended to be used by physicians in a clinical setting, in combination with other information related to the patient (such as clinical history, appearance, comorbidities, other scores, patient preferences, etc.) used in the context of the physician's decision to prescribe anticoagulant medication or to change an existing prescription. In addition, the calculator can be used repeatedly at patient follow-ups to assess the risk over time.

Clinical benefit

The ABC Bleeding Risk Score indicates whether additional measures should be provided to reduce the risk of bleeding as far as possible. The reduction of bleeding risk mainly aims at modifiable risk factors. When non-modifiable risk factors are present, physicians should decide to review the patient's risk factors more often for high bleeding risk patients. The ABC Bleeding Risk Score showed improved stratification between low and high risk patients, accurate risk estimations on model calibration, and improved net clinical benefit on decision curve analysis compared to the ESC guideline recommended HAS-BLED score.

Inclusion criteria

The calculator intended to be used for patients who have been diagnosed with either paroxysmal, persistent or permanent atrial fibrillation or atrial flutter with one or more of the following risk factors:

- Age ≥ 75 years;
- Age ≥ 65 years with coronary artery disease;
- Prior stroke, transient ischemic attack (TIA), or systemic embolus;
- Heart failure;
- Diabetes mellitus;
- Hypertension requiring pharmacologic treatment.

Exclusion criteria

The calculator should not be used for patients with one or more of the following characteristics:

- Severe heart valve disorder;
- Recent stroke;
- Creatinine clearance less than 25 mL/min;
- Active liver disease;
- Clinically significant mitral stenosis;
- Previous intracranial haemorrhage;
- Active alcohol or drug abuse.

User Profile

The calculator should **not** be used by patients.

The calculator may be used by physicians and qualified medical specialists in a clinical setting.

Intended Use Environment

The calculator 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 in Evidencio's mobile App. Furthermore, the calculator can be used through the Evidencio iFrame representation of the calculator, as an embedded view, provided that the specific Evidencio guidelines for iFrame implementations of this model are adhered to. The model is only intended for use in settings where the usage and result of a model are never urgently needed.

Functioning, physical principle

The calculator's underlying mathematical formula is a Cox-regression equation. The calculator uses a total of 6 different models using a combination of a Troponin biomarker and a kidney function biomarker. In addition, each model is able to calculate the risk over 1, 2, and 3 years.

J. Electronic label button

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 4.

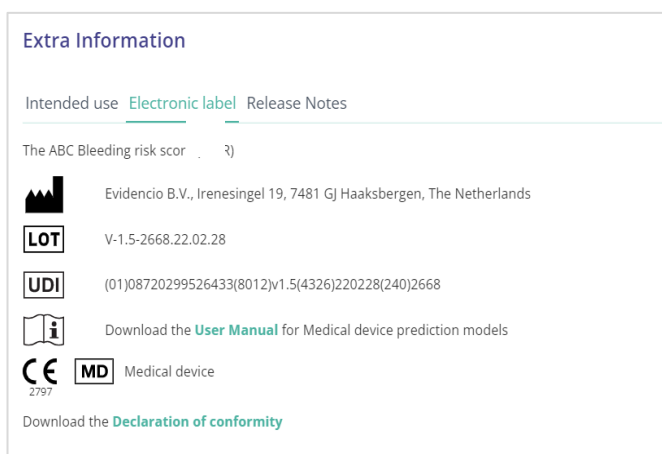


Figure 4. Example of the electronic label

K. Release notes

The 'Release Notes' button opens a pop-up with the latest release notes of the model. Here you can find what has changed over the last versions of the model. Additionally, if there are any known residual anomalies the user should be aware of, they are listed here.

L. User Manual

This user manual can be found in three places: 1) under the short description, 2) on the right of the model page, and 3) in the electronic label. 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 5. The user manual page is shown in Figure 6.

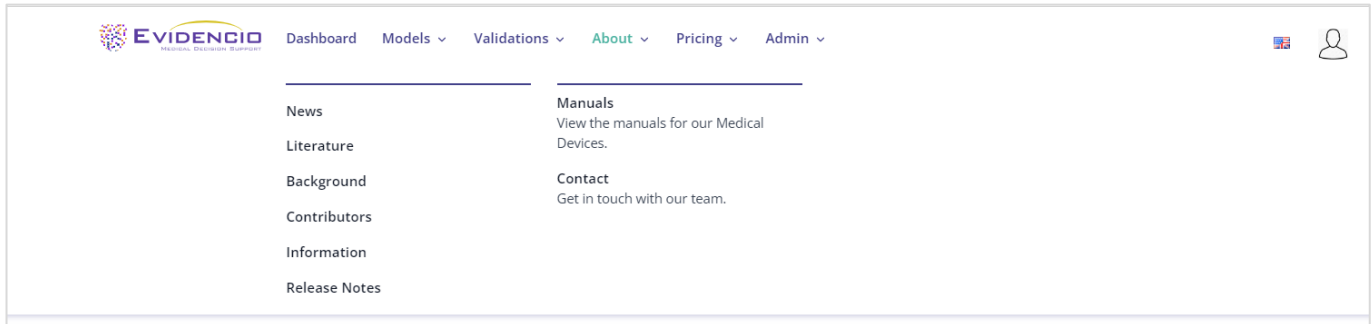


Figure 5. The drop-down menu where the user manual page can be found.

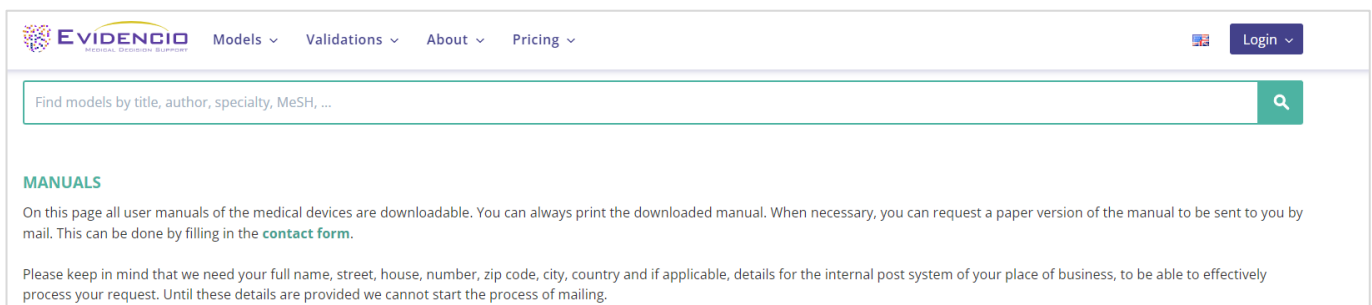


Figure 6. The user manual page for all user manuals.

You (The user) can always print this downloaded manual. When necessary, you can request a paper version of the manual to be sent to you by mail. Evidencio's contact details are listed in Chapter 6 of this user manual.

M. Input section

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

Categorical variables

In the example shown in Figure 7 and 8, the **Prior bleeding** variable concerns a categorical variable. The patient status can be entered by clicking on either button. The selected button changes to green, as seen in Figure 8.

Prior bleeding

Indicate whether the patient previously suffered from bleeding

No bleeding

Prior bleeding

Figure 7. The variable for Prior bleeding, where no button has been clicked, and thus no input has been provided by the user.

Prior bleeding

Indicate whether the patient previously suffered from bleeding

No bleeding
Prior bleeding

Figure 8. The variable for Prior bleeding, where the "Prior bleeding" button has been clicked.

Continuous variables

In the example shown in Figure 9, the **Age** variable, exemplifies a continuous variable. The plausible ranges for the variables are defined by the model author. For example, the model is not suitable for patients younger than 22, or older than 95. Thus, the model only allows input of ages for patients between the ages of 22 to 95.

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 65 is entered for **Age**).

Age

Age in years

22

95

65

 years

Figure 9. The variable for age, where "65" 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. In Figure 10, the details below **Troponin I** explain how the biomarker is measured in patients used to develop the model.

Troponin I

Cardiac troponin-I (cTnI-hs) concentrations were determined with high-sensitivity immunoassays on the ARCHITECT i1000SR (Abbott Diagnostics, Chicago, IL, USA)

2

1000

ng/L

Figure 10. An example on how additional information can be provided for a variable.

N. Result section

At the bottom of the page, the results of the model are shown.

Result calculation

When all variables are filled in, a result will be calculated. No risk is displayed until all variables are filled in. The result section indicates "Set all parameters to calculate prediction."

Result interpretation

In the result interpretation, a risk stratification is given based on the risk score. The patient is classified as high risk, medium risk or low risk. Furthermore, some explanation about the model is given including the c-index of the external validation. This information is also stated here below:

The current model calculates the risk of bleeding occurring within the next one, two, or three years. Even though the tool may support decisions involving the initiation of anticoagulant treatment, a high bleeding risk alone should not immediately lead to withholding anticoagulation.

The ABC bleeding risk score has been externally validated and compared head-to-head with similar prediction models such as the HAS-BLED score. The external validation of the ABC score resulted in a c-index of 0.69 (95% CI: 0.66 - 0.71) versus 0.62 (95% CI: 0.60 - 0.64) for the HAS-BLED score.

Depending on the selected biomarker, the model may perform slightly different. Still, all possible combinations of biomarkers resulted in similar model performance in terms of discrimination with C-indexes ranging between 0.68 and 0.71 on internal validation. Each of the six ABC bleeding risk score models performed better than the HAS-BLED score.

Relevant information for correct use of the model

At the bottom of the page, there is a link to Evidencio's terms and conditions of use, the privacy policy, and the disclaimer.

5. Use of Medical devices

In general, and unless explicitly stated otherwise, CE-marked tools on Evidencio are only to be used by physicians in a clinical setting, and are not for patient use.

To use the tool, Evidencio requires a stable internet connection and runs on the following devices:

- Personal computers or laptops using the following browsers:
 - Safari (the latest three versions)
 - Chrome (the latest three versions)
 - Firefox (the latest three versions)
 - Edge (the latest three versions)
- Tablets or smartphones running on the next operating systems:
 - IOS (the latest three versions)
 - Android (the latest three versions)

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 SaMD 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.

This model is only intended for use in settings where the usage and result of a model are never urgently needed.

6. 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.

Contact details of your competent authority can be found here: <https://www.ema.europa.eu/en/partners-networks/eu-partners/eu-member-states/national-competent-authorities-human>

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

File information:

Name: 2326-DOC-43 rev2.0 User manual SaMD - ABC Bleeding Risk Score Calculator.pdf
Size: 688813
Hash: EBC373CCEFDE75E5B52F9A9F561C90BA175D9D33AB2417618C56F60B99E0E100
Pages: 10
Date format: DD - MM - YYYY

Document history:

File created	27 - 07 - 2022 09:44:11 UTC	Created by D.S. (Ditte) Moejes (id: 6) IP: 192.168.1.50
File downloaded	27 - 07 - 2022 09:44:12 UTC	Viewed by D.S. (Ditte) Moejes (id: 6) IP: 192.168.1.50
File signatories	27 - 07 - 2022 09:44:24 UTC	Signatories: Author: D.S. (Ditte) Moejes (id: 6) Reviewer: E.M. (Emma) Knijn (id: 5) Approver: R.J. (Rob) Mentink (id: 2)
File downloaded	27 - 07 - 2022 09:45:52 UTC	Viewed by D.S. (Ditte) Moejes (id: 6) IP: 192.168.1.50
File signed	27 - 07 - 2022 09:45:56 UTC	Signed by D.S. (Ditte) Moejes (id: 6) IP: 192.168.1.50
File downloaded	27 - 07 - 2022 09:53:01 UTC	Viewed by E.M. (Emma) Knijn (id: 5) IP: 192.168.1.49
File signed	27 - 07 - 2022 09:53:06 UTC	Signed by E.M. (Emma) Knijn (id: 5) IP: 192.168.1.49
File downloaded	27 - 07 - 2022 09:54:12 UTC	Viewed by R.J. (Rob) Mentink (id: 2) IP: 192.168.1.37
File signed	27 - 07 - 2022 09:54:20 UTC	Signed by R.J. (Rob) Mentink (id: 2) IP: 192.168.1.37
File completed	27 - 07 - 2022 09:54:20 UTC	The document has been completed.