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7da80ef46b459f3b1097
d1c62e920a3179dd
62737b 0ec12f
e5e137a
fad
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3c66 f397b187ff 7ffc
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da81c1 1136f6
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91e
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Role: approver  
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ip: 192.168.1.53

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0ac3        cd49
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03113e890509b3d9
d15ccd 09cf41
b34f69a
7ef
```



# **User manual for GRACE Score**

**Version 1, MAY 2023, 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 GRACE Score. 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 immediately 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.** GRACE score for acute coronary syndrome (ACS) (MDR) Details

**B.** The Global Registry of Acute Coronary Events (GRACE) score estimates the risk of death or death/myocardial infarction (MI) in patients following an initial acute coronary syndrome (ACS). Intended use

**C.** Research authors: Keith A.A. Fox, Omar H. Dabbous, Robert J. Goldberg, Karen S. Pieper, Kim A Eagle, Frans Van de Werf, Alvaro Avezum, Shaun G. Goodman, Marcus D. Flather, Frederick A. Anderson Jr., Christopher B. Granger Electronic label

**D.** Draft | Cardiology | R-Script model Release Notes

**E.** LOT V-1.2-3449.23.02.20 User manual

**F.** UDI (01)08719327522707(8012)v1.2(4326)230220(240)3449

**K.** Download the User manual for Medical device prediction models and consult the Intended use.

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**L.**

Age: 45 Year

Heart rate: 60 Beats per minute

Systolic blood pressure: 105 mmHg

Killip class:  II

Creatinine value:  Known

Creatinine: 0.5 mg/dl

Cardiac arrest at presentation:  No

Elevated troponin or other necrosis cardiac biomarkers:  Yes

ST-segment deviation:  No

GRACE version:  GRACE 2.0

Calculated risk of death in 6 months is: **2.6 %**

---

**M.** Calculated risk of death in 6 months is: **2.6 %**

See details below.

	Risk % (Points)
In hospital	1.1
To 6 months	2.6 ( 86 )
1 year	3
1 year death/MI	7.8
3 years	3.9

The GRACE risk tool can be used to predict the cumulative risk of death and death or myocardial infarction.

Validation of the GRACE score on the FAST-MI 2005 cohort showed adequate levels of discrimination with C-indices ranging from 0.78 to 0.82.

Different International guidelines recommend the use of the GRACE risk score as risk assessment in patients with acute coronary syndrome using the GRACE score was shown to be superior to the (subjective) physician assessment for the occurrence of death or myocardial infarction.

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

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. 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 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>

### 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.

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

### Details

Model author	Evidencio.Medical.Devices	Rating	★ ★ ★ ⓘ
Model ID	3449	Status	<span style="border: 1px solid #ccc; padding: 2px;">Draft</span>
Version	1.2	Share	<span style="border: 1px solid #ccc; padding: 2px; margin-right: 5px;">f</span> <span style="border: 1px solid #ccc; padding: 2px; margin-right: 5px;">t</span> <span style="border: 1px solid #ccc; padding: 2px;">in</span>
Revision date	2023-02-20		
Specialty	Cardiology		
Model type	R-Script model <small>(Calculation)</small>		
MeSH terms	<ul style="list-style-type: none"> <li>Acute Coronary Syndrome</li> <li>Myocardial Infarction</li> <li>Creatinine</li> <li>Blood Pressure</li> <li>Pulse</li> </ul>		

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

<p><b>Title or description</b></p> <p>Original article: Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE)</p> <p>Update 2.0: Should patients with acute coronary disease be stratified for management according to their risk? Derivation, external validation and outcomes using the updated GRACE risk score DOI: 10.1136/bmjopen-2013-004425</p> <p>NICE guideline Acute coronary syndromes (NG185)</p> <p>ESC Clinical Practice Guidelines (2020 Acute Coronary Syndromes (ACS) in Patients Presenting without Persistent ST-Segment Elevation (Management of) Guidelines)</p>	<p><b>Tags</b></p> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">External validation</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Internal validation</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Peer review</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">External validation</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Internal validation</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Peer review</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Paper</div> <div style="border: 1px solid #ccc; padding: 2px; margin-bottom: 2px;">Information on topic</div> <div style="border: 1px solid #ccc; padding: 2px;">Information on topic</div>
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### Related files

No related files available

Figure 3. An example of Supporting publications & related files.

## H. 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 GRACE Score the following intended use is described:

### Intended use

The device is intended to be used by healthcare professionals to estimate the 6-month risk of death and death/myocardial infarction in patients with acute coronary syndrome (ACS) or those who are highly suspected to have ACS.

The device combines a patient's Heart rate, Age, Systolic blood pressure, Killip class, Creatinine value, and whether there was Cardiac arrest at presentation, Elevated Troponin, and a ST-segment deviation to calculate the 6-month risk of death and death/myocardial infarction.

The device is intended to be used for patients with acute coronary syndrome (ACS) or those who are highly suspected to have ACS, by healthcare professionals and qualified medical specialists in a clinical setting, in combination with other information related to the patient (such as clinical history, appearance, comorbidities, other scores, patient preferences, etc.). The device is not intended for use by patients on their own.

The GRACE score is not intended to replace clinical decision-making, it can only **inform** the healthcare professional, and only provides a 6-month risk of death and death/myocardial infarction. No direct instructions for further diagnostics, treatment, or otherwise, are given.

### Clinical benefit

The GRACE score is intended to assist patients with relevant and specified clinical outcome parameters. Concretely, this is achieved by estimating a risk in order to support clinical decision making aimed at patients with acute coronary syndrome (ACS) or those who are highly suspected to have ACS, in order to support clinical decision making regarding patient triage. Correct functioning of the GRACE score can result in these clinical benefits:

- The GRACE score can assist in risk stratification for patients.
- Risk stratification can reduce the burden of (invasive and intensive) medical procedures such as tests on patients with low risks, reducing, shortening or avoiding stays in hospitals or other care facilities.
- Risk stratification can reduce the unnecessary consumption of (scarce) medical resources, decreasing costs and increasing their availability for high risk patients.

### Intended target population and exclusion

The GRACE Score is intended to be used only for a specific group of patients, corresponding to the below indications and contra-indications. Additionally, for the use of the GRACE Score on Evidencio, the patient's age should be at least 18 years and not exceed 100 years.

### Clinical indication

The GRACE Score is intended for:

- patients with ACS or those who are highly suspected to have ACS.

### Contra-indications

The GRACE Score should not be used for patients that do not fulfill the inclusion criteria, i.e. it is not intended for:

- patients without ACS or those who are not suspected to have ACS.

### User profile

Since mortality and myocardial infarction are regarded as a 'critical healthcare situation or condition', the use of the SaMD is intended for specialised trained users. Thus, the SaMD may be used by healthcare professionals and qualified medical specialists in a clinical setting. Healthcare professionals do not require additional training prior to the use of the medical device. The SaMD should not be used by patients.

### Intended Use Environment

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

## Functioning, physical principle

The SaMD's underlying mathematical formula is a Cox-regression equation. The acquisition and processing of the data, the analyses to assemble the relevant criteria for the SaMD as well as the setup and refinement of the GRACE 1.0 and 2.0 score are described in the original studies from Fox et al. from 2006 and Fox et al. from 2014 for the GRACE 1.0 and GRACE 2.0 score. Entering the details of an individual in the Evidencio SaMD initiates the calculation 6-month risk of death, and displays the risk of in-hospital/6-month death and death or MI and its associated risk category (low, moderate, high).

### I. 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.

**Extra Information**

Intended use [Electronic label](#) [Release Notes](#)

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GRACE score for acute coronary syndrome (ACS) (MDR)

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

 V-1.2-3449.23.02.20

 (01)08719327522707(8012)v1.2(4326)230220(240)3449

 Download the [User manual](#) for Medical device prediction models

 Medical device

Download the [Declaration of conformity](#)

Figure 4. Example of the electronic label

### J. 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.

### K. 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.

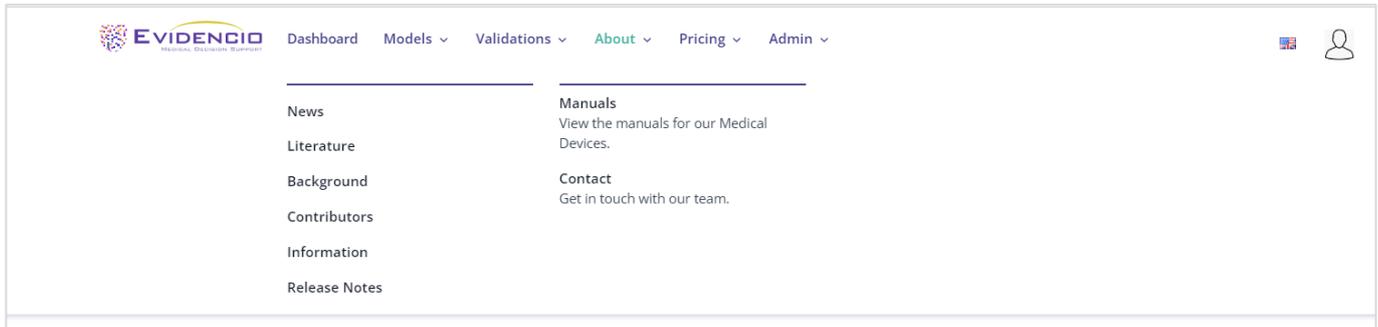


Figure 5. The drop-down menu where the user manual page can be found.

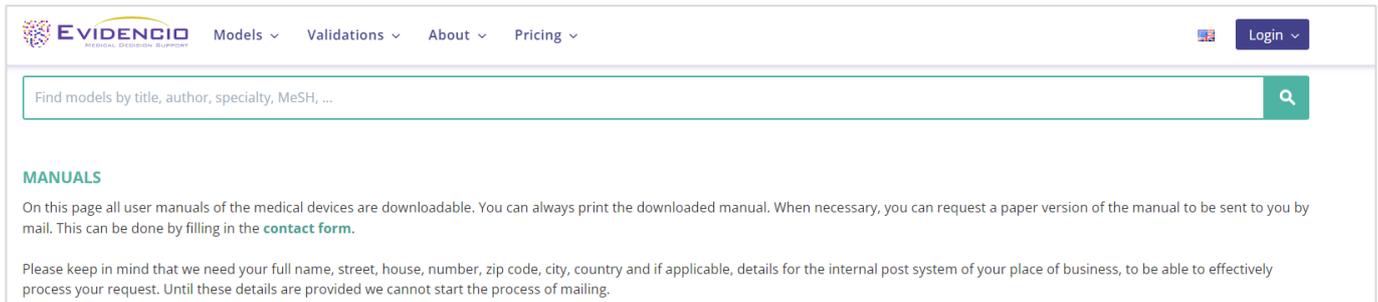


Figure 6. The user manual page for all user manuals.

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.

## L. Input section

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

### Categorical variables

In the example shown in Figure 7, the **ST-segment deviation** variable concerns a categorical variable. The patient status can be entered by clicking on either button. The selected button changes to green.



Figure 7. The variable for Prior bleeding, where the “Prior bleeding” button has been clicked.

### Continuous variables

In the example shown in Figure 8, the **Age** variable, exemplifies a continuous variable. For example, the model is not suitable for patients younger than 18, or older than 100. Thus, the model only allows input of ages for patients between the ages of 18 to 100.

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**).



Figure 8. 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 9, the details below **Troponin I** explain how the biomarker is measured in patients used to develop the model.

**Elevated troponin**

Or other necrosis cardiac biomarkers

Figure 9. An example on how additional information can be provided for a variable.

### M. 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. Furthermore, some explanation about the model is given. An example of the information is shown In Figure 10.

Calculated risk of death in 6 months is: **24.6 %**

See details below.

	Risk % (Points)
In hospital	15.9
To 6 months	24.6 ( 160 )
1 year	25.2
1 year death/MI	30.7
3 years	53.9

The GRACE risk tool can be used to predict the cumulative risk of death and death or myocardial infarction.

Validation of the GRACE score on the FAST-MI 2005 cohort showed adequate levels of discrimination with C-indices ranging from 0.78 to 0.82.

Different international guidelines recommend the use of the GRACE risk score as risk assessment in patients with acute coronary syndrome using the GRACE score was shown to be superior to the (subjective) physician assessment for the occurrence of death or myocardial infarction.

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

Figure 10. The result information

#### 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 immediately 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](http://www.evidencio.com)

tel: +31 53 85195 08

e-mail: [info@evidencio.com](mailto:info@evidencio.com)

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File completed	<b>01 - 06 - 2023</b> 08:29:15 UTC	The document has been completed.