User manual for the INFLUENCE 3.0

Version 3, January 2026, in English

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1. The Evidencio platform

The Evidencio platform facilitates the creation, use, validation and implementation of medical prediction algorithms and clinical decision support tools. This User Manual specifically relates to the INFLUENCE 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 certain CE-marked information, calculators, equations, and algorithms (tools) on any of its websites, applications, apps, or services. These tools may only be used in accordance with the intended use / intended purpose that has been published with the respective CE-marked tool.

In general, and unless explicitly stated otherwise, CE-marked tools on Evidencio are only to be used by healthcare professionals and are not for patient use.

The CE-marked content on the platform is to be regarded as a specific set of tools, apart from the general platform content. Any available content, on any of the websites, applications, apps, or services provided by Evidencio that is not clearly labelled as a CE-marked tool is explicitly not covered by this disclaimer for CE-marked content, the general Evidencio Disclaimer for non-CE-marked content applies.
CE-marked tools may provide limited professional advice to the intended user(s). However, the intended user must exercise their clinical judgment as to the information these tools provide.

Evidencio does not assume any liability or responsibility for damage or injury (including death) to you, other persons, or property arising from any misuse of any product, information, idea, or instruction contained in the tools provided to you.

The disclaimer for non-CE-marked content is available on the Evidencio website: https://www.evidencio.com/disclaimer.

Your use of the websites, applications, apps, or services provided by Evidencio is subject to our Terms & Conditions, which can be found here: https://www.evidencio.com/terms-conditions.

⚠ 3. Warnings for CE-marked content

Calculations alone should never dictate patient care, and are no substitute for professional judgement. See our full disclaimer on: https://www.evidencio.com/disclaimer. This tool is only to be used by healthcare professionals, 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 algorithm is only intended for use in settings where the usage and result of an algorithm are never immediately needed.

This algorithm is only intended for curatively treated non-metastatic breast cancer patients, and never pre-treatment. Do not base treatment decisions on the results of this tool. It is only intended for decision support for follow-up procedures after breast cancer treatment.

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

3.1. Notice to the user

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.

4. Device Description INFLUENCE 3.0

The INFLUENCE 3.0 is a flexible algorithm to predict time-dependent individual risks of locoregional recurrence and secondary contralateral tumors at a 5-year scale; it can support clinical decision-making regarding personalized follow-up strategies for curatively treated non-metastatic breast cancer patients.

4.1. Lifetime, residual risks and side effects

The INFLUENCE 3.0 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 algorithm 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 algorithm.

The INFLUENCE 3.0 is a low-risk Medical Device Software (MDSW), there are no noticeable risks involved outside of possible mis-estimation of patient's time-dependent risks of locoregional recurrence, 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 algorithm 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*.

The INFLUENCE 3.0 does not have any direct side effects.

5. Electronic Label

The electronic label of this device contains the following information:

CE 2797	**Name of the device**	INFLUENCE 3.0: Risk of Locoregional recurrence, secondary contralateral tumors
	Manufacturer information	Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
LOT	**LOT number**	V-3.13-2238.26.02.03
UDI	**UDI number**	(01)08720299526440(8012)v3.13(4326)260203(240)2238
MD	**MD indication**	Medical device

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

5.2. UDI number

Stands for Unique Device Identifier (UDI) number is an international tool that helps users identify and find information on products. Evidencio's UDIs 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 use

6.1. Intended purpose

The INFLUENCE 3.0 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 time-dependent risk of locoregional recurrence and second primary contralateral breast cancer for curatively treated non-metastatic breast cancer patients.

The device is intended to be used for curatively treated non-metastatic breast cancer patients. The result of the INFLUENCE 3.0 is intended to be reviewed and interpreted *by/together with healthcare professionals*, as well as being used for a patient selection aid, to allow patient and healthcare professional to come to an informed decision regarding the planning of follow-up care.

The INFLUENCE 3.0 is not intended to replace clinical decision-making, it can only provide information to the user on the estimation of the risks of locoregional recurrence and Second primary contralateral breast cancer. The user can use this information to support clinical decision-making regarding personalised surveillance. In practice, this typically entails decisions surrounding time between follow-up meetings.

The INFLUENCE 3.0 is explicitly **not** meant to be used for treatment decision-making, because information on treatment in the algorithm was derived from a retrospective database, meaning that treatment allocation was not random.

6.2. Clinical benefit

The INFLUENCE 3.0 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 curatively treated non-metastatic breast cancer patients, in order to support clinical decision-making regarding patient prognosis. Correct functioning of the INFLUENCE 3.0 can result in the following clinical benefit:

- The INFLUENCE 3.0 can assist in risk stratification for patients.

6.3. Intended target population and exclusion

The INFLUENCE 3.0 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 INFLUENCE 3.0 should be used for patients who meet the following inclusion criteria:

- Women surgically treated for primary invasive nonmetastatic breast cancer
- Patients should be at least 18 years or older

6.3.2. Clinical contra-indications

The INFLUENCE 3.0 should not be used for patients who meet one or more of the following exclusion criteria:

- Patients with synchronous breast cancer
- Male patients
- Patients whose breast cancer was detected through incidental findings
- Patients with positive tumor margins after surgery
- Patients with Hereditary Breast Cancer
- Patients younger than 18 years old

There is an extra exclusion criteria for the NST Group:

- Patients who only received neoadjuvant radiation therapy or targeted therapy without chemotherapy.

6.4. Intended users

The intended users are healthcare professionals. Results shall always be reviewed and interpreted by healthcare 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. Users can manually enter the required input data through the user interface. In addition, the MDSW is available as an embedded view via Evidencio's iFrame representation. 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. History/ versions of the algorithm

The version of the INFLUENCE 3.0 concerns an update of the INFLUENCE 2.0 Algorithm, which has been previously certified as a class I medical device under the MDD. Both concern the version of which Evidencio is the manufacturer.

6.8. Functioning, physical principle

The MDSW's underlying mathematical formula is a combination of Random Survival Forest models and Cox regression models. Entering the details for an individual in the MDSW initiates the estimation of the risks of locoregional recurrence and second primary contralateral breast cancer.

7. Additional information

7.1. Details

Algorithm author	T.A. Hueting
Algorithm ID	2238
Version	3.13
Revision date	03-FEB-2026
Speciality	Oncology
Algorithm type	R-Script algorithm
MeSH terms	Breast Cancer

7.2. Input variables

To perform the calculations successfully, the INFLUENCE 3.0 requires the input variables as listed in **Table 1**, for patients with neoadjuvant treatment, and in **Table 2** the input variables for patients without neoadjuvant treatment are listed.

Table 1. Variables used as input for the INFLUENCE 3.0 for patients with neoadjuvant treatment.

Name	Description	Type	Range (step size)	Units
Age	Age at the time of diagnosis	Continuous	18 – 100 (1)	Years
Method of detection	Method by which the cancer was detected	Categorical	Symptoms Screening	-
DCIS component	Presence of ductal carcinoma *in situ*	Categorical	No Yes	-
Axillary lymph node dissection	Axillary Lymph Node Dissection (ALND) was performed	Categorical	No Yes	-
Pathologic complete response	Absence of invasive cancer cells in breast tissue and axillary lymph nodes, upon pathological examination following NST	Categorical	No Yes	-
Sublocalisation	Location of the primary tumour in the breast	Categorical	Outer quadrants Inner quadrants Central parts Overlapping lesions	-
Differentiation grade	Grade of differentiation in the tumour	Categorical	Grade 1 Grade 2 Grade 3	-
HER2 status	Presence of Human Epidermal growth factor Receptor 2	Categorical	Negative Positive	-
Hormone receptor status	If either Estrogen Receptor (ER) or Progesterone Receptor (PR)	Categorical	Negative Positive	-

	or both are positive, fill in Positive, otherwise negative			
Hormonal therapy	Was the patient treated with hormonal therapy	Categorical	No Yes	-
Relapse free time	How many months the patient has been relapse free	Continuous	0 – 33 (3)	Months
Zoom chart	Adjust the charts' margins to the calculated risks	Categorical	No Yes	-
Show confidence intervals	Report the 95% confidence intervals	Categorical	No Yes	-

Table 2. Variables used as input for the INFLUENCE 3.0 for patients without neoadjuvant treatment.

Name	Description	Type	Range (step size)	Units
Age	Age at the time of diagnosis	Continuous	18 – 100 (1)	Years
Method of detection	Method by which the cancer was detected	Categorical	Symptoms Screening	-
Tumor stage	Pathological tumour stage	Categorical	pT1 pT2 pT3 pT4	-
Nodal stage	Pathological nodal stage	Categorical	pN0 pN1 pN2 pN3	-
Sublocalisation	Location of the primary tumour in the breast	Categorical	Outer quadrants Inner quadrants Central parts Overlapping lesions	-
Histological tumor type	Classification of the tumour based on histological growth pattern	Categorical	Ductal Lobular Mixed Other	-
Differentiation grade	Grade of differentiation in the tumour	Categorical	Grade 1 Grade 2 Grade 3	-
HER2 status	Presence of Human Epidermal growth factor Receptor 2	Categorical	Negative Positive	-
Hormone receptor status	If either Estrogen Receptor (ER) or Progesterone Receptor (PR) or both are positive, fill in Positive, otherwise negative	Categorical	Negative Positive	-
Surgery	Which breast cancer surgery was performed	Categorical	Breast conserving surgery Mastectomy	-
Direct reconstruction[A] (Only when Surgery is set to Mastectomy)	Was a direct reconstruction performed during mastectomy	Categorical	No Yes	-
Chemotherapy	Was the patient treated with chemotherapy	Categorical	No Yes	-
Radiotherapy	Was the patient treated with radiotherapy	Categorical	No Yes	-
Hormonal therapy[B] (only visible when Hormone receptor status is set to "Positive")	Was the patient treated with hormonal therapy	Categorical	No Yes	-

Anti-HER2 therapy[C] (Only when HER2 status is set to Positive)	Trastuzumab	Categorical	No Yes	-
Relapse free time	How many months the patient has been relapse free.	Continuous	0 – 33 (3)	Months
Zoom chart	Adjust the charts' margins to the calculated risks	Categorical	No Yes	-
Show confidence intervals	Report the 95% confidence intervals	Categorical	No Yes	-

[A]"Direct reconstruction" is only visible when "Surgery" is set to "Mastectomy". [B]"Hormonal therapy" is only visible when "Hormone receptor status" is set to "Positive". [C]"Anti-HER2 therapy" is only visible when "HER2 status" is set to "Positive".

7.3. Formula

The INFLUENCE 3.0 consists of a combination of Random Survival Forest models and Cox regression models. As Random Survival Forests are a ***black box*** and there are 100 bootstrap samples used for the Cox regression model, it is not possible to reproduce the mathematical equations in this document. The original process for the development of the algorithm is described in the derivation paper by Maaren et al., 2024.

7.4. Result interpretation

The output of the INFLUENCE 3.0 consist of multiple different calculated risks. For better visualisation for some of these risk graphs are provided. One of the input options is to indicate whether the user would like to see the 95% confidence intervals (CI) of these calculated risks.

The 5-year risk for **locoregional recurrence** and the 5-year risk for **contralateral primary breast cancer** are provided per year and cumulatively (for 3- and 5-years post-surgery). Both risks are visualised per year in a point graph up to year 5 after surgery, which also contain the 95% CI when selected. The contralateral primary breast cancer per-year risk is conditional, in that it only applies to patients which did not have an event in one of the previous years. The cumulative 3- and 5-year risk are also provided with or without the 95% CI dependent on the selected option.

Waffle charts for both risks are also provided, which indicate how many women, out of a 100 with the same characteristics, will have a locoregional recurrence and how many will have a 2nd primary breast tumour within 3-years after surgery.

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.

7.5. Study characteristics

The calculated results are based on algorithms that have been developed using data of 59.785 patients who have been treated for breast cancer in the Netherlands. The performances of the algorithms have been evaluated on discrimination and calibration using 100 bootstrap samples.

The C-index for locoregional recurrence and contralateral breast cancer were respectively 0.77 (95% CI 0.77 – 0.77) and 0.68 (95% CI 0.67 – 0.68), for patients who did not receive neoadjuvant treatment.

The C-index for locoregional recurrence and contralateral breast cancer were respectively 0.77 (95% CI 0.76 – 0.78) and 0.73 (95% CI 0.69 – 0.76), for patients who received neoadjuvant treatment.

Regarding calibration, observed-predicted differences were all <1%. In the data used to develop the algorithm, the following event rates were observed:

- **Locoregional recurrence**
  - n = 1090 (2.2%) for patients who did not receive neoadjuvant treatment
  - n = 334 (3.3%) for patients who received neoadjuvant treatment
- **Contralateral breast cancer**
  - n = 1566 (3.2%) for patients who did not receive neoadjuvant treatment
  - n = 199 (2.0%) for patients who received neoadjuvant treatment
- **No event**

- n = 46975 (94.6%) for patients who did not receive neoadjuvant treatment
- n = 10154 (94.8%) for patients who received neoadjuvant treatment

7.6. Supporting publication & Related files

The INFLUENCE 3.0 development and function is similar to the INFLUENCE 2.0, the derivation study which is described by Völkel *et al*. (2021).

When found, relevant newly found publications will be added here. These publications have tags to identify their link with the algorithm. Examples of relevant tags are; "Peer review", "Internal validation", "External validation", and "TRIPOD". Publications that have the tags: "Internal validation" or "External validation", contain data on the performance characteristics of the device.

Table 3. Overview of selection of supporting publications & Related files.

INFLUENCE 3.0 Derivation paper	**The INFLUENCE 3.0 model: updated predictions of locoregional recurrence and contralateral breast cancer, now also suitable for patients treated with neoadjuvant systemic therapy** *MC van Maaren, TA Hueting, DJP van Uden, M van Hezewijk, L de Munck, MAM Mureau, PA Seegers, QJM Voorham, MK Schmidt, GS Sonke, CGM Groothuis-Oudshoorn, S Siesling, NABOR project group* DOI: 10.1016/j.breast.2024.103829
INFLUENCE 2.0 Derivation paper	**Improved risk estimation of locoregional recurrence, secondary contralateral tumors and distant metastases in early breast cancer: the INFLUENCE 2.0 model** Vinzenz Völkel, Tom A Hueting, Teresa Draeger, Marissa C van Maaren, Linda de Munck, Luc J A Strobbe, Gabe S Sonke, Marjanka K Schmidt, Marjan van Hezewijk, Catharina G M Groothuis-Oudshoorn, Sabine Siesling DOI: 10.1007/s10549-021-06335-z

7.7. Release notes

The release notes for each publicly available version of the device can be found on the Evidencio website page for the INFLUENCE 3.0: https://www.evidencio.com/models/show/2238, selecting the correct (version of the) 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 algorithm version is selected.

8. Implementation of the algorithm through an API

The INFLUENCE 3.0 can be used through Evidencio's API to allow for (automated) calculation of the 5-year risk for **locoregional recurrence** and the 5-year risk for **contralateral primary breast cancer** per year and cumulatively (3- and 5-years since surgical treatment). In the case of use of the MDSW through the API, the user should take into account the different inputs for the algorithm, 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.

9. Using the algorithm on the Evidencio website

Using the tool on the Evidencio website requires a stable internet connection. The tool was developed to work on the four most commonly used internet browsers; Google Chrome (version 135.0.7049.115 and higher), Mozilla Firefox (version 137.0.2 and higher), Microsoft Edge (version 135.0.3179.98 and higher), and Apple Safari (version 18.4 and higher). The medical device cannot be used in combination with Internet Explorer.

The tool can also be accessed on mobile devices running the most recent versions of the Android (version 15 and higher) and iOS (version 18.4.1 and higher) operating systems.

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

The personal computers, laptops, tablets or smartphones used should at least be able to have an internet connection and use the browsers mentioned above.

Furthermore, the algorithm 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 algorithm are adhered to.

The Evidencio MDSW algorithms 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 minimal screen 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 algorithm is only intended for use in settings where the usage and result of an algorithm are never immediately needed.

9.1. General algorithm landing page

The medical device model on the Evidencio platform is shown in **Figure 1**. The algorithm landing page contains the following sections, that are indicated in **Figure 1**.

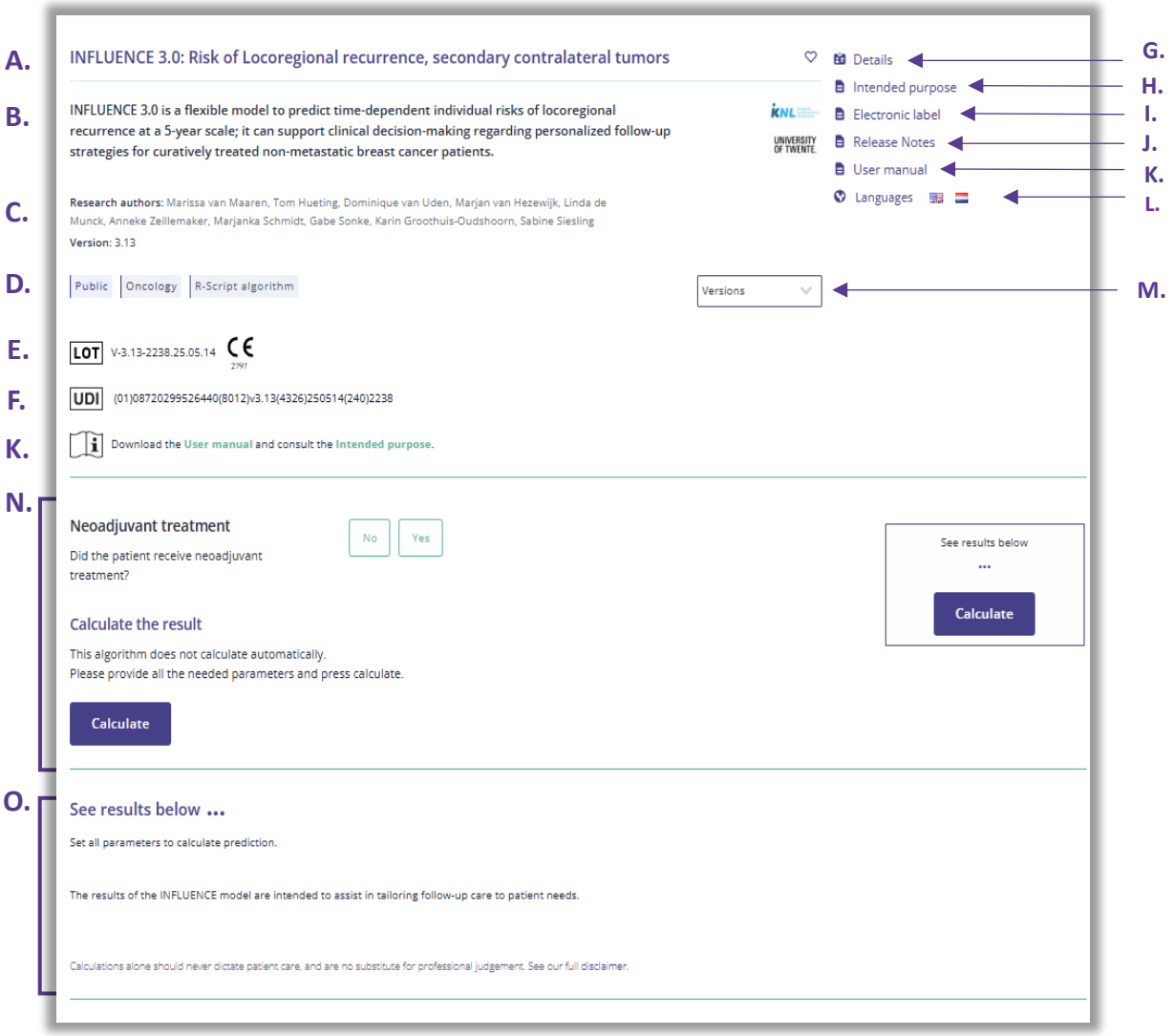

Figure 1. Example of an algorithm landing page on the Evidencio website.

A. Algorithm title

This is the title and name of the algorithm.

B. Algorithm description

This is a short description of the algorithm.

C. Research authors

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

D. Algorithm tags

These are the tags that are assigned to the algorithm. Evidencio has the following status tags: “Draft”, “Public”, “Private”, “Under review”. Evidencio has the following algorithm type tags: “Composite model”, “Sequential model”, “API model”. Evidencio has the following calculation method tags: “Linear regression”, “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 algorithm version, the algorithm identifier, and the algorithm 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

For information on the UDI Number see **Section 5.2** on **page 5** of this user manual.

G. Details button

On the top right of the algorithm 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 algorithm. 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 algorithm as shown in **Figure 2**.

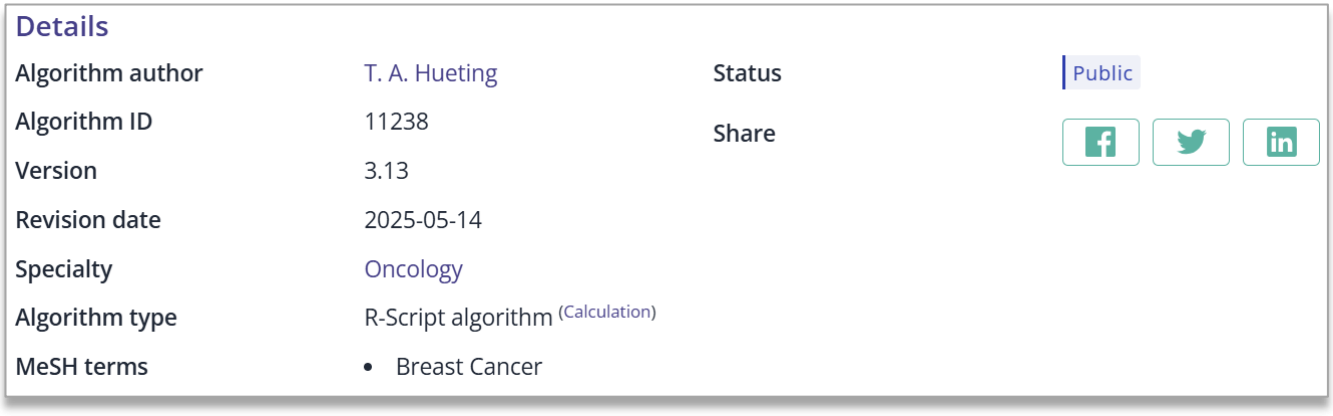

Figure 2. Example of first part of detail section.

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 algorithm. Additional information is provided on the methods used to develop and/or validate the algorithm. An example of the Study characteristics section can be seen in **Figure 3**.

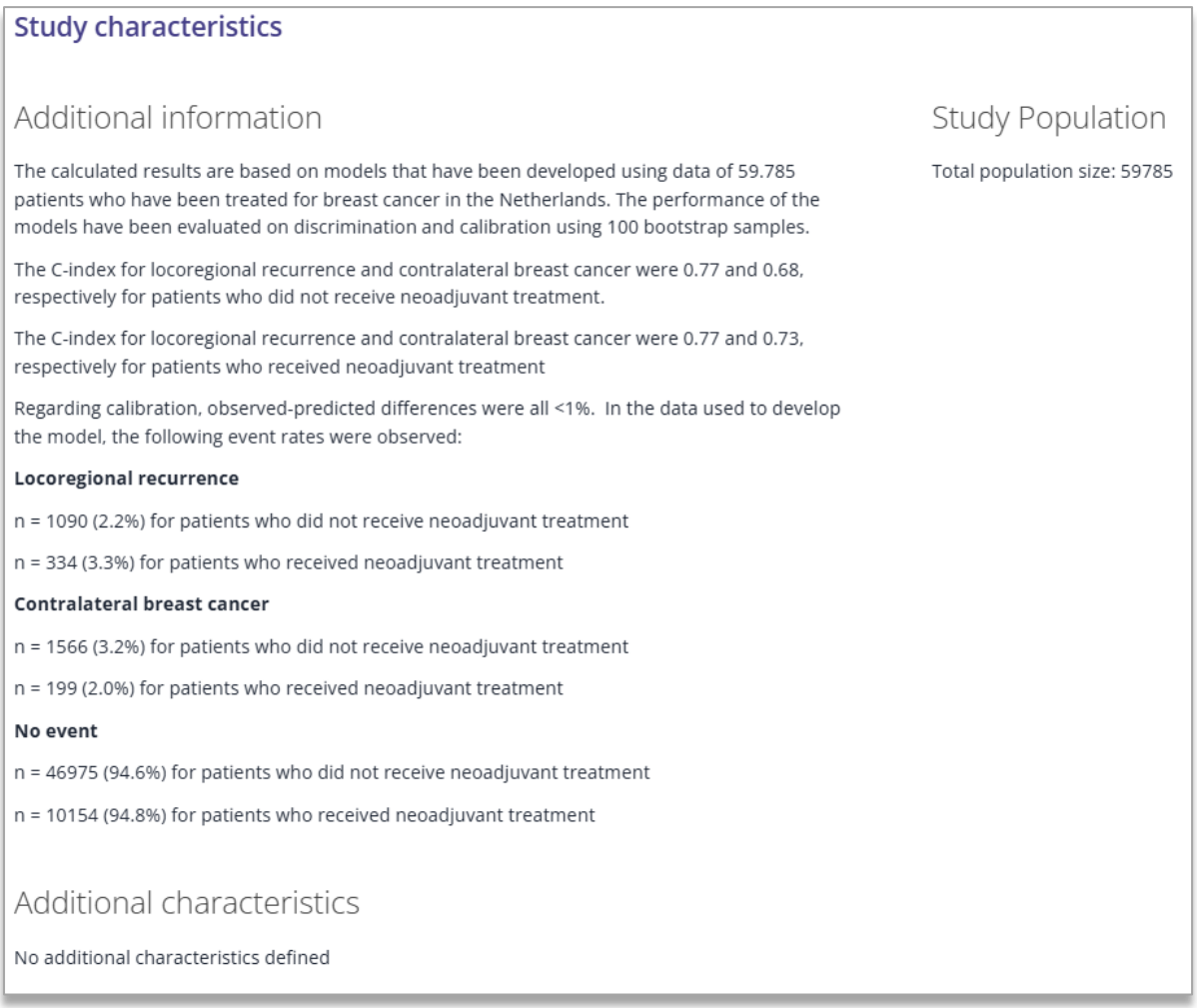

Figure 3. Example of the study characteristics section under the Details tab.

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**.

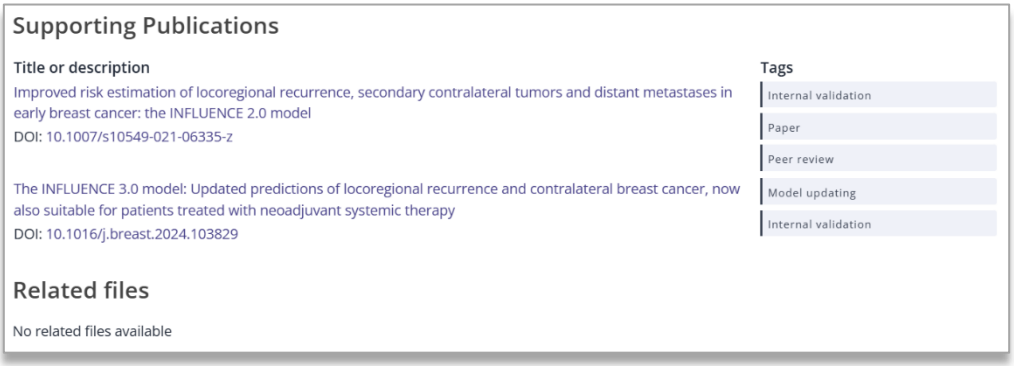

Figure 4. Example of the Supporting publication & Related files section under the Details tab.

Tags are attached to the different files to identify their link with the algorithm. 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 algorithm, its user, target population, clinical benefit, etc. This information is also provided in this manual and can be found in **Chapter 6** on **page 5**.

I. Electronic label

The electronic label button opens a pop-up with the location and address of Evidencio, the LOT number, the UDI number, the CE-mark, the medical device logo and a download link for the declaration of conformity of the medical device. The example of the electronic label is shown in **Figure 5**.

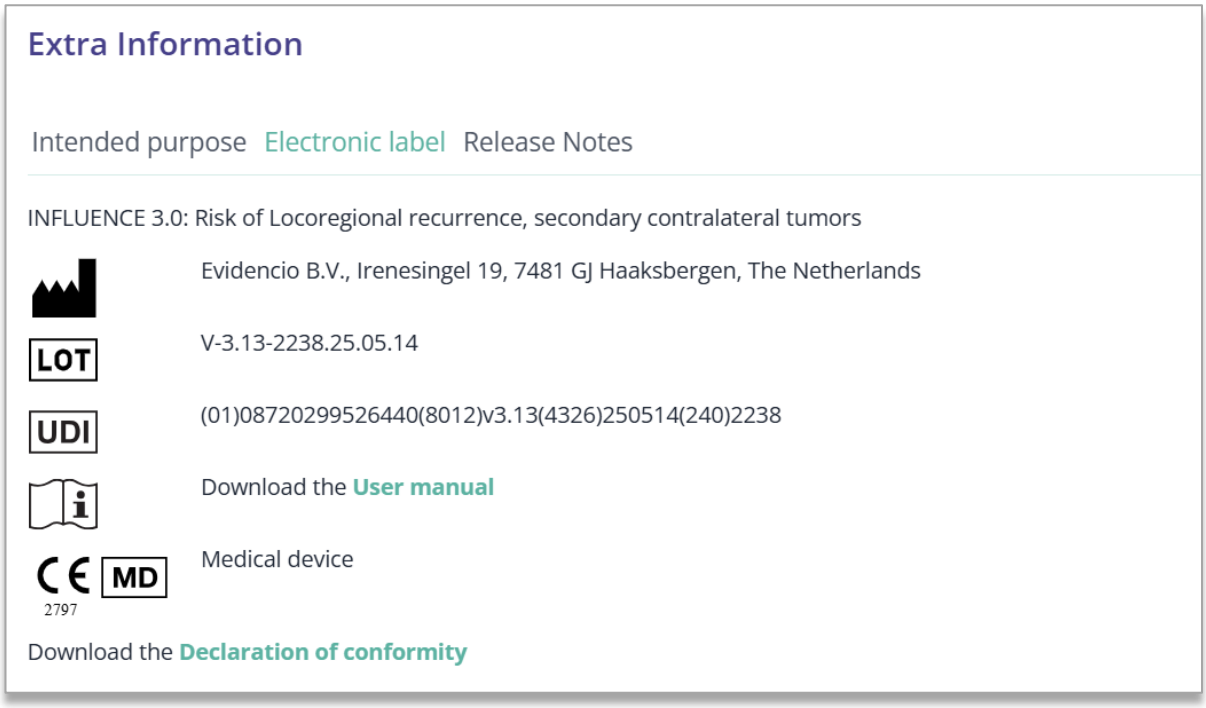

Figure 5. Example of an electronic label under the Electronic Label tab.

J. Release notes

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

The 'Release Notes' button opens a pop-up with the latest release notes of the algorithm. Here you can find a list of the most significant changes over the different versions of the algorithm. 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 algorithm on the Evidencio algorithm page, 2) on the right of the algorithm 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 10** of this user manual.

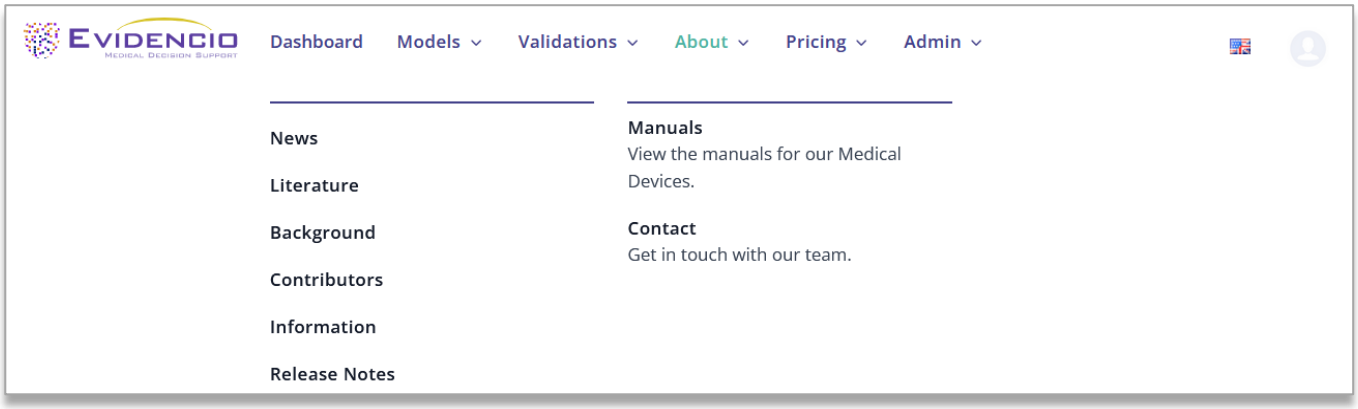

Figure 6. The drop-down menu where the user manual page can be found.

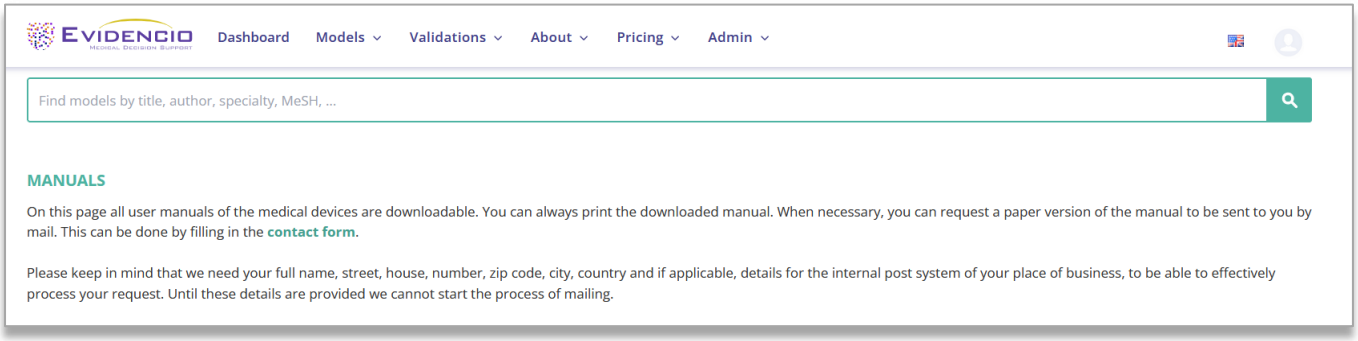

Figure 7. The user manual page for all user manuals.

L. Languages

Here an overview of languages in which the INFLUENCE 3.0 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 algorithm 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 INFLUENCE 3.0 for a list as displayed in **Figure 8**. Please note that the algorithm currently selected is not presented in the dropdown menu.

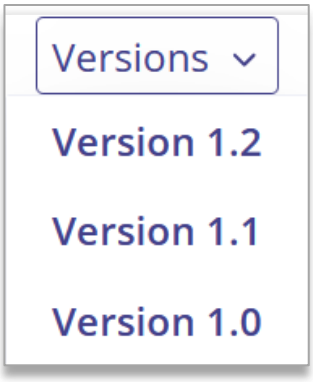

Figure 8. Example of version selection tab.

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**.

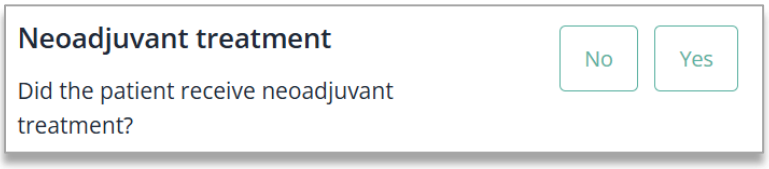

Figure 9. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.

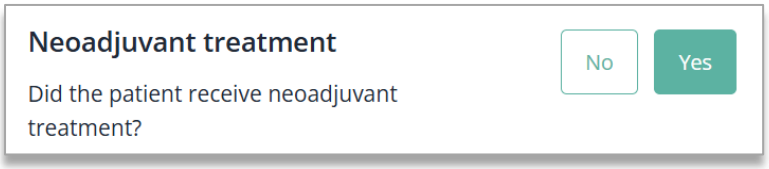

Figure 10. Example of a categorical variable, where the "Yes" button has been clicked.

Continuous variables

In the example shown in **Figure 11**, the **Continuous Variable 3**, exemplifies a continuous variable. The plausible ranges for which the algorithm 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 50 years is entered for the **Continuous Variable 3**).

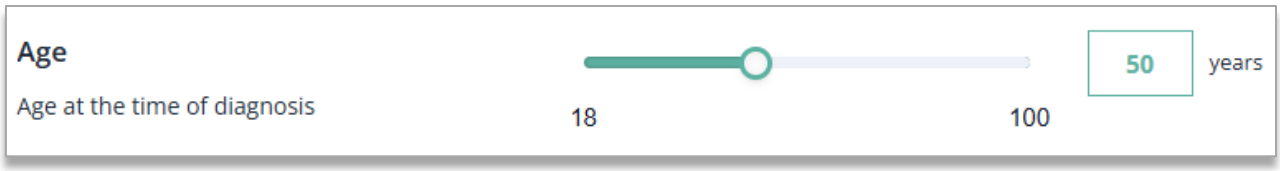

Figure 11. Example of a continuous variable, where “50 years” has been entered.

Details on variable measurements

Directly underneath the name for each variable, additional details can be provided (see **Figure 11)**, for example, 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 algorithm 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, and the user selects “Calculate”, 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 12**.

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

10. User manual revision history

Version	Revision notes
V1.0 MAY-2024	Original version
V2.0 OCT-2024	Added Device Description
V3.0 FEB-2026	Updated the user manual for V3.13 of the INFLUENCE 3.0 (which added the 3-year risk).

11. Manufacturer details

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