User manual
for the
Prostate Health Index (PHI)

Version 1.0, March 2026, in English

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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 Prostate Health Index (PHI). The User Manual can also be referred to as the Instructions For Use (IFU). The Prostate Health Index (PHI) meets the requirements laid down in: Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. Compliance with the applicable regulations is provided by means of declaration of conformity.

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.

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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, 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.

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 Prostate Health Index (PHI)

The Prostate Health Index (PHI) is a prediction algorithm based on three prostate biomarkers that can accurately estimate the probability of (clinically significant) prostate cancer. This can aid in decision making prostate cancer (PCa) management and treatment.

The Algorithm is Medical Device Software (MDSW), hosted on the Evidencio platform.

The calculation of the algorithm is performed by communication with the Evidencio platform, hosted at www.evidencio.com. The algorithm is also accessible by 3rd party applications through the API and iFrame implementation. The Evidencio platform is managed under Evidencio's certified quality management system that ensures the correctness of calculations and availability of its services.

The Summary of Safety and Performance for this device will be made available via EUDAMED once the relevant module is fully operational. In the meantime, the Summary of Safety and Performance can be requested from the manufacturer and will be provided without undue delay.

4.1. Lifetime, residual risks and side effects

The Prostate Health Index (PHI) 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 Prostate Health Index (PHI) is a low-risk device, there are no noticeable risks involved outside of possible mis-estimation of patient risk for (clinically significant) prostate cancer, 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 erroneous calculations or the inaccessibility of the Prostate Health Index (PHI) due to a technical error, have been mitigated when possible.

These measures focused 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 Prostate Health Index (PHI) 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**	Prostate Health Index (PHI)
▲	**Manufacturer information**	Evidencio B.V., Irenesingel 19, 7481 GJ Haaksbergen, The Netherlands
LOT	**LOT number**	V-1.0-10531.26.03.25
UDI	**UDI number**	(01)08720938015175(8012)v1.0(4326)260325(240)10531
IVD	**IVD indication**	*In vitro* diagnostic medical device

The electronic label can be found on the Evidencio website, see also section **I** and **Figure 5** in **Chapter 10**.

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, which is an international tool that helps users identify and find information on products. Evidencio's UDI's have the following format:

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

The UDI-DI (Device Identifier) number is a unique numeric code. For each medical device of Evidencio, a unique UDI-DI is ascribed. This UDI-DI is used as an "access key" for information stored in a unique device identification database (UDID). Information on Evidencio's medical devices can be found by searching for the UDI-DI number in the following data base: https://gepir.gs1.org/index.php/search-by-gtin.

6. Intended purpose

6.1. Intended use

The Prostate Health Index (PHI) is medical device software (MDSW) intended to be used to estimate the probability of (clinically significant) prostate cancer in men aged 50 years or older with a Prostate Specific Antigen (PSA) value between 2.0 and 10.0 ng/mL. PHI combines Total PSA, Free PSA and [-2]proPSA to calculate the probability of prostate cancer. The input variables require a blood sample from the patient. PHI automates the calculation of the formula. It requires quantitative inputs to provide a quantitative output.

PHI is not intended to replace clinical decision-making, it can only provide information to the healthcare professional on the estimation of the probability of (clinically significant) prostate cancer. The healthcare professional can use this information to support clinical decision-making regarding the need for further diagnostic evaluation of the patient. In practice, this typically entails the decision to perform a prostate biopsy or magnetic resonance imaging (MRI).

6.2. Clinical benefit

The benefits and risks associated with the use of the Prostate Health Index (PHI) for the patient are indirect. The benefits arise from clinical decisions made using the Prostate Health Index (PHI) in combination with other clinical and patient-specific factors. The Prostate Health Index (PHI) can result in the following clinical benefits:

- The Prostate Health Index (PHI) can assist in risk stratification for patients.
- Digital implementation of the algorithm underlying the Prostate Health Index (PHI) as a medical device can improve the speed and reliability of calculation.

6.3. Intended target population and exclusion

The result of the Prostate Health Index (PHI) is intended to be reviewed and interpreted by medical specialists only. The device is not intended for use by patients on their own.

6.3.1. Clinical indications

The Prostate Health Index (PHI) should be used for patients who meet the following inclusion criteria:

- Men aged >50 years.
- PSA value between 2.0 and 10.0 ng/mL using the Beckman Coulter Hybritech calibration.

6.3.2. Clinical contra-indications

The Prostate Health Index (PHI) is not intended to be used for:

- Patients who use medication known to affect PSA levels.

6.4. Intended users

The intended users are healthcare professionals. Results shall always be reviewed and interpreted by healthcare professionals, 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. The device is not intended to be used at the bedside of the patient.

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 MDSW

The version of the Prostate Health Index (PHI) concerns the initial version of the MDSW of which Evidencio is the manufacturer.

7. Result interpretation

The primary output of this device is given as: **The Prostate Health Index (PHI) score is: [#]%**

Table 1. Probabilities of PCa when using Beckman Coulter Hybritech Calibration as found by Catalona *et al.* (2011).

Prostate Health Index (PHI) score	Interpretation
>24.9	Probability of PCa is **11.0%** (95% confidence interval: **6.5%** - **15.8%**)
25.0 - 34.9	Probability of PCa is **18.1%** (95% confidence interval: **13.7%** - **22.6%**)
35.0 – 54.9	Probability of PCa is **32.7%** (95% confidence interval: **27.3%** - **38.0%**)
>55.0	Probability of PCa is **52.1%** (95% confidence interval: **42.0%** - **62.1%**)

Conditional information

The cut-offs values and corresponding probabilities of (clinically significant) prostate cancer are derived from the widely cited validating paper of Catalona *et al.* (2011) using the Beckman Coulter Access Hybritech PSA Calibrators. Optimal cut-offs and probabilities differ between patient populations, such as (but not limited to) patients eligible for biopsy or radical prostatectomy, regions, PSA calibrators, and patient ethnicities. Please consult local clinical guidelines or external validation studies to choose the appropriate cut-off and probability.

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.

Additional remarks on the conditional information.

The Prostate Health Index (PHI) has been frequently studied since its development and validated across various regions. It can be used to support decision-making in different stages of the diagnostic pathway of PCa. The use case and region of use require different cut-off values to achieve the best performance of the Prostate Health Index (PHI). The use of the Prostate Health Index (PHI) before prostate biopsy is the most extensively studied use case. The derivation paper divided the scores into four ranges and calculated the probability of PCa for each range with a 95% CI. These ranges with their corresponding probabilities for PCa were also used in the implementation of the algorithm by Evidencio.

8. Additional information

8.1. Details

Algorithm author	T. A. Hueting
Algorithm ID	10531
Version	1.0
Revision date	2026-MAR-25
Speciality	Oncology, Urology
Algorithm type	Custom calculation
MeSH terms	• Prostate Cancer

8.2. Input variables

To perform the calculations successfully, the Prostate Health Index (PHI) requires the input variables as listed in **Table 2**.

Table 2. Variables used as input for the Prostate Health Index (PHI).

Name	Description	Type	Range (step size)	Units
Total PSA	Prostate-Specific Antigen.	Continuous	2.0 - 10.0 (0.1)	*ng/mL*
Free PSA	Free Prostate-Specific Antigen is the unbound variant of PSA.	Continuous	0.1 - 4.0 (0.1)	*ng/mL*
[-2]proPSA	[-2]proPSA is a PSA isoform which is associated with PCa.	Continuous	0.1 - 100 (0.1)	*pg/mL*

Formula

The formula used by the algorithm is as follows:

$$PHI = \left(\frac{"[-2]proPSA"}{"Free\ PSA"} \right) * \sqrt{"Total\ PSA"}$$

8.3. Study characteristics

The Prostate Health Index (PHI) is developed by Beckman Coulter and validated by Jansen *et al.* in 2010 and Catalona *et al.* in 2011. Before the development of the Prostate Health Index (PHI), Prostate Antigen Serum (PSA) was commonly used as a screening in asymptomatic men. PSA with a cutoff at 4.0 ng/mL was used to decide if prostate biopsy was necessary or not. However, PSA may be confounded by benign conditions and showed therefore a low specificity. The Prostate Health Index (PHI) combines PSA, free PSA (the unbound form of PSA), and [-2]proPSA and is developed to increase the specificity in predicting PCa. The Prostate Health Index (PHI) is externally validated in many studies and demonstrated better performance in predicting prostate cancer compared to PSA serum alone.

A large number of scientific studies, reviews, and-meta reviews have demonstrated the use of the Prostate Health Index (PHI) during different phases of prostate cancer treatment. For this wide variety of cut-off values and corresponding clinical endpoints have been used, often in combination with other diagnostic information. Evidencio only provides the interpretation provided in the original derivation paper and thus only information on that validation cohort.

In **Table 3** information on the characteristics of the patient data used to derive and validate the algorithm is provided.

Table 3. This table contains information on the patient group data used to validate the algorithm by Catalona *et al*. (2011).

Name	p-value		Benign	Cancer
Age (Years)	0.477	Median	63.0	63.0
		Mean	62.6 ± 7.0	63.0 ± 7.1
		Range	50 – 84	50 – 84
Race, n(%)	0.025	Caucasian	361 (78.1)	365 (84.9)
		African-American	24 (5.2)	22 (5.1)
		Other	22 (4.8)	9 (2.1)
		Unknown	55 (11.9)	34 (7.9)
Ethnicity, n(%)	0.059	Hispanic	14 (3.0)	6 (1.4)
		Not Hispanic	187 (40.5)	153 (35.6)
		Unknown	261 (56.5)	271 (63.0)
Prostate volume	<0.001	Median	51.0	40.0
		Mean ± SD	55.1 ± 23.2	44.3 ± 19.4
		Range	16 – 209	14 – 120
Prior biopsy, n(%)	<0.001	No prior biopsy	345 (74.7)	361 (84.0)
		Prior biopsy	105 (22.7)	54 (12.6)
		Unknown	12 (2.6)	15 (3.5)
Gleason Score, n(%)	N/A	5	N/A	1(0.2)
		6	N/A	289 (67.2)
		7	N/A	119 (27.7)
		8	N/A	9 (2.0
		9	N/A	11 (2.6)
		Unknown	N/A	1 (0.1)
PSA (ng/mL)	0.199	Median	5.1	5.3
		Mean ± SD	5.3 ± 1.9	5.4 ± 1.9
		Range	2.0 – 10.0	2.0 – 9.8
fPSA (ng/mL)	<0.001	Median	1.0	0.7
		Mean ± SD	1.0 ± 0.5	0.9 ± 0.5
		Range	0.1 – 4.3	0.2 – 3.9
[-1]proPSA (ng/mL)	0.003	Median	12.9	14.1
		Mean ± SD	14.4 ± 7.1	16.8 ± 11.1
		Range	2.9 – 43.5	2.9 – 93.5
%fPSA	<0.001	Median	18.8	15.1
		Mean ± SD	20.0 ± 8.0	16.4 ± 7.6
		Range	3.1 – 53.2	3.7 – 51.1
Prostate Health Index (PHI)	<0.001	Median	30.3	42.2
		Mean ± SD	33.9 ± 15.0	49.2 ± 31.3
		Range	13.7 – 98.2	10.2 – 325.8

8.4. Supporting publication & Related files

Several relevant studies, such as the original derivation study by Catalona *et al*. (2011) are contained in **Table 4**. Evidencio has provided tags to these publications 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 4. Overview of selection of supporting publications & Related files.

External validation	**A Multicenter Study of [-2]Pro-Prostate Specific Antigen Combined With Prostate Specific Antigen and Free Prostate Specific Antigen for Prostate Cancer Detection in the 2.0 to 10.0 ng/ml Prostate Specific Antigen Range** (2011) *William J. Catalona, Alan W. Partin, Martin G. Sanda, John T. Wei, George G. Klee, Chris H. Bangma, Kevin M. Slawin, Leonard S. Marks, Stacy Loeb, Dennis L. Broyles, Sanghyuk S. Shin, Amabelle B. Cruz, Daniel W. Chan, Lori J. Sokoll, William L. Roberts, Ron H.N. van Schaik, Isaac A. Mizrahi* DOI: 10.1016/j.juro.2010.12.032
External validation	**Prostate-specific antigen (PSA) isoform p2PSA in combination with total PSA and free PSA improves diagnostic accuracy in prostate cancer detection (2010)** *Flip H Jansen, Ron H N van Schaik, Joep Kurstjens, Wolfgang Horninger, Helmut Klocker, Jasmin Bektic, Mark F Wildhagen, Monique J Roobol, Chris H Bangma, Georg Bartsch* DOI: 10.1016/j.eururo.2010.02.003
Systematic Review	**Prostate health index (PHI) as a reliable biomarker for prostate cancer: a systematic review and meta-analysis** *Agnello L, Vidali M, Giglio RV, Gambino CM, Ciaccio AM, Lo Sasso B, Ciaccio M.* DOI: 10.1515/cclm-2022-0354
Systematic Review	**Diagnostic Accuracy of Liquid Biomarkers for Clinically Significant Prostate Cancer Detection: A Systematic Review and Diagnostic Meta-analysis of Multiple Thresholds** (2023) *Kawada T, Shim SR, Quhal F, Rajwa P, Pradere B, Yanagisawa T, Bekku K, Laukhtina E, von Deimling M, Teoh JY, Karakiewicz PI, Araki M, Shariat SF.* DOI: 10.1016/j.euo.2023.10.029

8.5. Analytical performance characteristics

To demonstrate the analytical performance of the Prostate Health Index (PHI), evidence was collected based on five requirements. This led to the following results:

- A code review and functional test showed that the calculation of the online tool provides the exact same results as described by the developer Beckman Coulter.
- Monthly uptime reports show that the device is available online with an uptime of at least 99%.
- The calculation time is within 2 minutes, otherwise an error is given to the manufacturer, this is analysed each 6 months in the analysis of quality data.
- Absence of unacceptable cybersecurity vulnerabilities.
- On a scale from 1 to 5, where 5 means that users trust the implementation very much, the reliability score was 4.44, and the accuracy score was 4.56 on average.

8.6. Clinical performance characteristics

In literature, the use and interpretation of the Prostate Health Index (PHI) is quite heterogeneous, using a broad variety of different in- and exclusion criteria between studies. It has been shown that the Prostate Health Index (PHI) can be used to stratify patients according to risk of (clinically significant) prostate cancer in a wide variety of patients (e.g. further screening in patients with a heightened PSA, monitoring during active surveillance, in combination with multiparametric MRI imaging.) Performance is slightly different for these different populations and use cases, but acceptable for the different groups. However, score thresholds and associated sensitivity and specificity will differ, and no consensus on proper thresholds exists within the scientific literature.

Statistical performance characteristics

A pooled meta-analysis by Agnello *et al*. was performed on a total of 14255 patients from a total of 60 studies, in which they pooled true/false positives and true/false negatives together. The authors found a sensitivity of 0.79 (95% CI 0.74-0.83) and a specificity of 0.63 (95% CI 0.56 – 0.69) for PCa and a sensitivity of 0.87 (95% CI 0.80 – 0.92) and specificity of 0.57 (95% CI 0.46 – 0.67) for clinically significant PCa (csPCa).

A systematic review by Kawada *et al*. (2023) including a total of 8652 patients identified a sensitivity of 0.85 (95% CI 0.80-0.89) and specificity of 0.52 (95% CI 0.43-0.60) with an AUC of 0.78 in the overall population. For the biopsy-naïve subgroup of 6236 patients, performance was slightly different with a sensitivity of 0.87 (95% CI 0.81-0.91) and a specificity of 0.57 (95% CI 0.50-0.63) in csPCa prediction.

Benefit assessment

Several studies have been performed on the potential clinical benefit of the Prostate Health Index (PHI) using Decision Curve Analysis (DCA). These studies show a higher net benefit at all relevant thresholds than the current state-of-the art (total PSA) as well as [-2]proPSA and free PSA when compared using Decision Curve Analysis. The clinical net benefit of Prostate Health Index (PHI) combined with MRI, as opposed to total PSA combined with MRI, has also been demonstrated in decision curve analysis in literature.

There have been multiple studies into the cost-effectiveness of using the Prostate Health Index (PHI) compared to using PSA-screening alone. Use of the Prostate Health Index (PHI) contributed to a reduced number of negative biopsies, a relative reduction in the total number of diagnoses, and a lower total cost of screening compared to total PSA alone.

8.7. Release notes

The release notes for each publicly available version of the device can be found on the Evidencio website page for the Prostate Health Index (PHI): https://www.evidencio.com/models/show/10531, selecting the correct device (version), 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.

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 latest versions, as of the making of this manual, of the four most commonly used internet browsers; Google Chrome (version 136.0.7103.114 and higher), Mozilla Firefox (version 139.0.1 and higher), Microsoft Edge (version 137.0.3296.52 and higher), and Apple Safari (version 18.4 and higher). The medical device cannot be used in combination with Internet Explorer.

Use of the Evidencio platform is always encrypted through the https protocol.

The tool can also be accessed on mobile devices running the most recent versions of the Android (version 15.0 and higher) and iOS operating systems (version 18.5).

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

An example of a medical device algorithm interface on the Evidencio platform is shown in **Figure 1**. The different sections indicated are explained in this chapter.

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 algorithm", "Sequential algorithm", "API algorithm". Evidencio has the following calculation method tags: "Linear regression", "Logistic regression", "Cox regression", "RScript" and "Custom calculation". 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**. 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.

Details

Algorithm author	Evidencio	Status	Draft
Algorithm ID	10513	Share	
Version	1.0		
Revision date	2025-02-11		
Specialty	Cardiology , Geriatrics , Vascular medicine		
Algorithm type	Custom calculation (Conditional)		
MeSH terms	• Heart Failure • Diabetes Mellitus • Elderly		

Condition	Formula
Categorical Variable 1 = Yes	$\text{Categorical Variable 1} + \text{Categorical Variable 2}^2 + \dfrac{3 \cdot \text{Continuous Variable 1}}{\text{Continuous Variable 2}}$
Categorical Variable 1 = No	$\sqrt{\text{Continuous Variable 1}} + \dfrac{2 \cdot \text{Continuous Variable 2}}{\text{Continuous Variable 3}}$

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**.
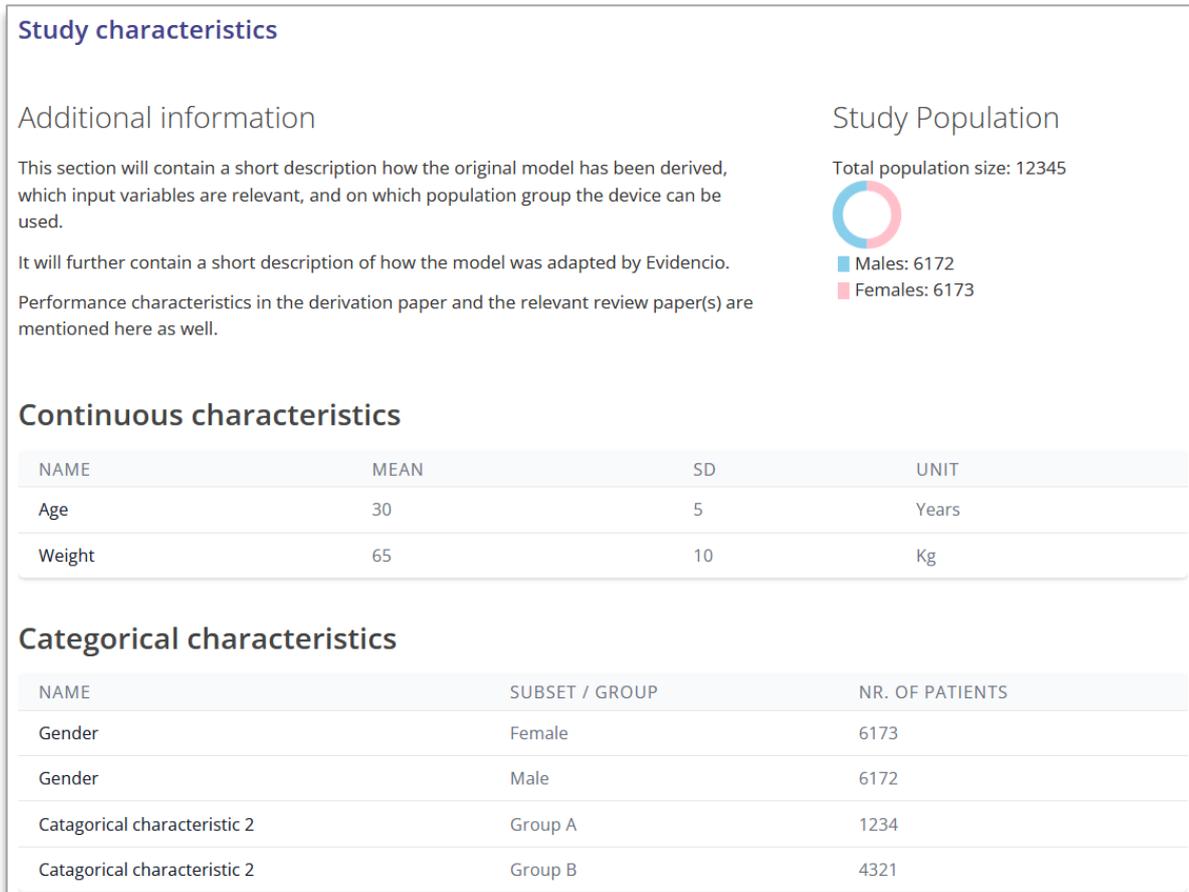

Figure 3. Example of the study characteristics section under the Details tab.

Figure 4. Example of the Supporting publication & Related files 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. The list of related files and relevant tags can also be found in **§8.4**. These sections can be found at the bottom of the Details-pop-up as shown in **Figure 4**.

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**.
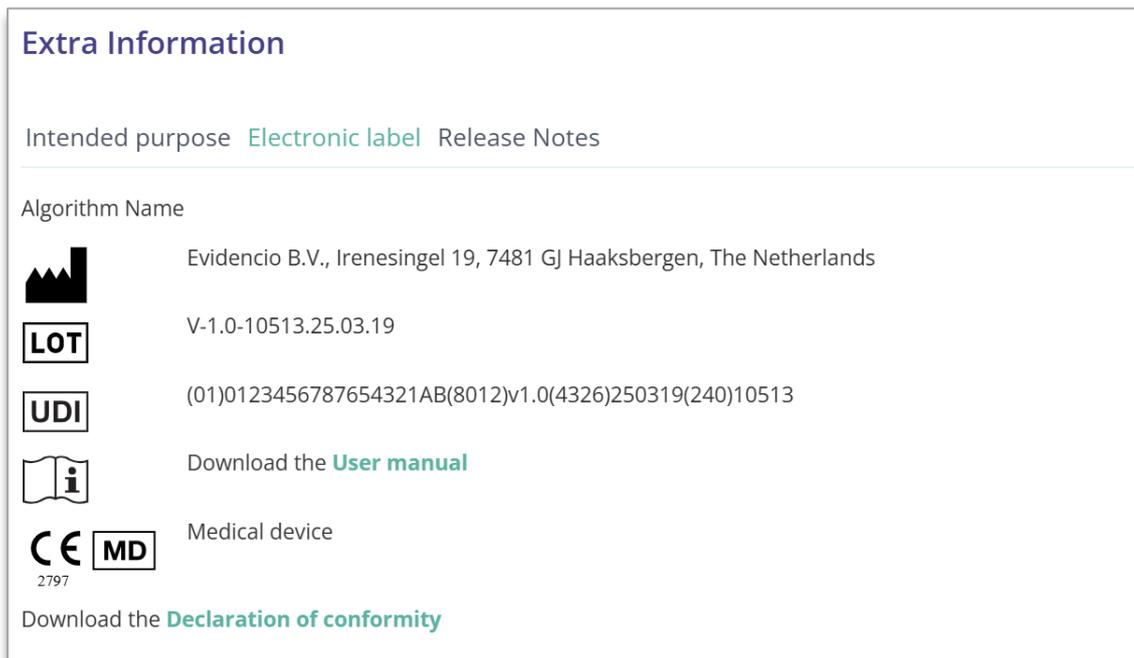

Figure 5. Example of an electronic label under the Electronic Label tab.

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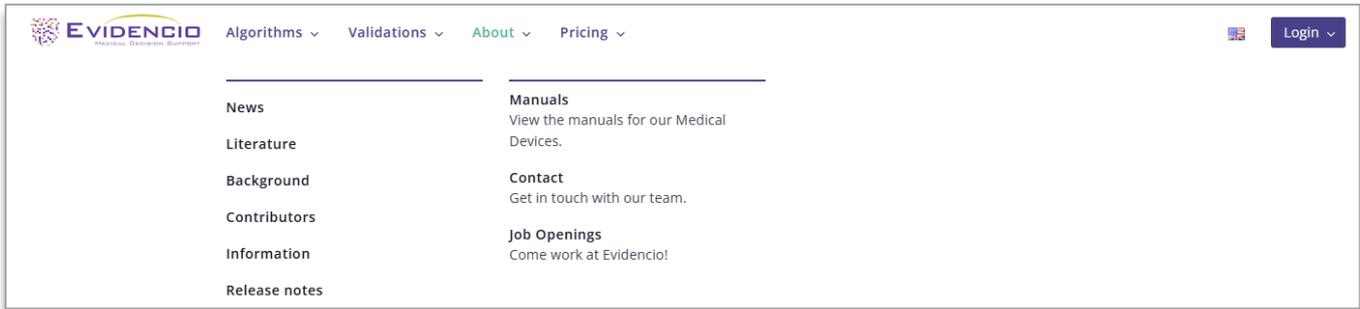
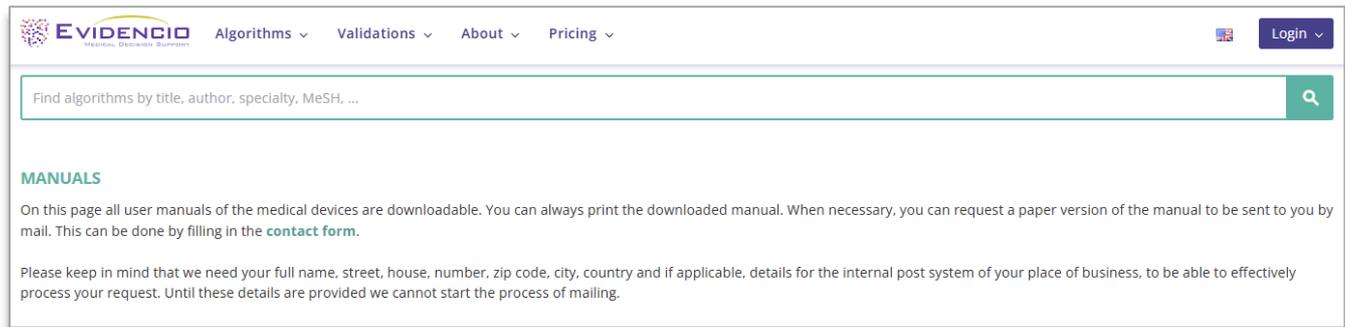**Figure 6.** The drop-down menu where the user manual page can be found.

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

L. Languages

Here an overview of languages in which the Prostate Health Index (PHI) 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.

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 Prostate Health Index (PHI) from 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**.
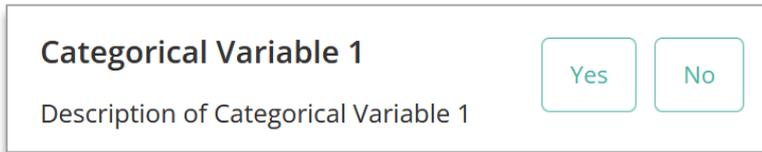

Figure 9. Example of a categorical variable, no button has been clicked and thus no input has been provided by the user.
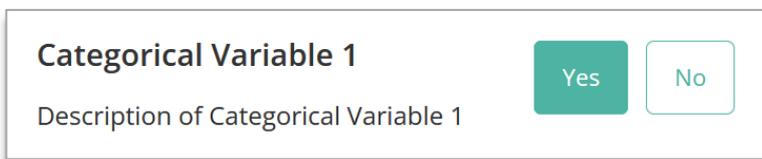

Figure 10. Example of a categorical variable, where the "Yes" button has been clicked.

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 10.2 mg/dL is entered for the **Continuous Variable 3**).

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

Unit conversion

Sometimes it is possible to use a unit conversion, by clicking on the unit when the green arrows are present. See **Figure 12** below where the unit has been clicked and switched.
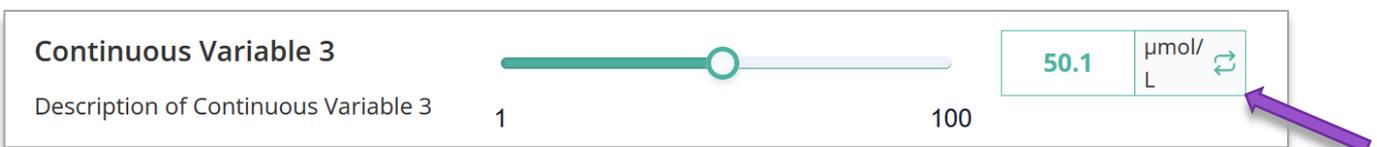
Figure 12. Example of a continuous variable where "50.1 $\mu mol/L$" has been entered.

Details on variable measurements

Directly underneath the name for each variable, additional details can be provided on, 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 (cut-off values).

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 presses calculate, a result can be calculated. No result is displayed until all variables are filled in and the result section will indicate; *"Set all parameters to calculate prediction."*

Result interpretation

In the result interpretation, a stratification may be provided based on the calculated results. Additional information about this stratification and the classification as found in the derivation and important validation cohorts may also be provided. An example of the information is shown in **Figure 13**.

The result of the algorithm's calculation is: ... points.

Set all parameters to calculate prediction.

Here a short section will be provided to help with the result interpretation. This piece of text can be general for all results, or can be shown depending when the certain conditions are met.

This can include statement into which the risk classification the calculated result can be stratified (e.g. **High**, **Moderate**, **Low**).

Also the performance data in the Internal and relevant External validation cohorts can be shown here such as but not limited to; the c-satistic, sensitivity, specificity together with the number of cases of the condition in scope within the cohort.

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

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

10. Implementation of the algorithm through an API

The Prostate Health Index (PHI) can be used through Evidencio's API to allow for (automated) calculation of the (clinically significant) prostate cancer. 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.

The information provided over the API is the same as the information that is displayed in the graphical user interface on the web application provided by Evidencio. In **Box 1** below, an example of a result from the Prostate Health Index (PHI) over the API is shown. The result concerns a JSON formatted text. The API for the PHI leverages the generic API that is provided for the Evidencio platform and therefore contains information that may be applicable for different software algorithms and devices. This means that not all of the details provided over the API may be relevant for the PHI.

```json
{    "CIPercentage": 0,
  "id": 10531,
  "author": "T. A. Hueting",
  "title": "Prostate Health Index (PHI)",
  "variables": {
     "9364529982": 3.6,
     "5405729676": 1.3,
     "6567159834": 20.1
  },
  "min": 29.3,
  "max": 29.3,
  "additionalResultSet": [],
  "mintxt": "29.3",
  "maxtxt": "29.3",
  "result": "29.3",
  "resultText": "The Prostate Health Index (PHI) score is:",
  "postresultText": "",
  "formulaSegments": [],
  "conditionalResultArray": [
     "<p><p>Due to the Prostate Health Index (PHI) being between 25 and 35, the probability of cancer is estimated to be 18.1% (95%
confidence interval: 13.7% - 22.6%) according to Catalona et al. (2011)</p></p>"
  ],
  "conditionalResultText": "<p><p>Due to the Prostate Health Index (PHI) being between 25 and 35, the probability of cancer is estimated to
be 18.1% (95% confidence interval: 13.7% - 22.6%) according to Catalona et al. (2011)</p></p>",
  "UDI": "(01)08720938015175(8012)v1.0(4326)260320(240)10531",
  "medicalDevice": "This is an in vitro diagnostic medical device. The electronic label is available at:
https://www.evidencio.com/models/show/10531?v=1.0",
  "userManual": "Always refer to the user manual for correct use of the in vitro diagnostic medical device. The user manual can be found at:
https://www.evidencio.com/manuals"
}
```

Box 1: Example of an API output for the PHI.

Table 5 shows a match between the separately listed items in the API output with the items listed on the graphical user interface on the Evidencio website (elaborated in **Chapter 9**).

Table 5. Agreement between the API output and the graphical user interface on the Evidencio website.

API Item	GUI item	Comment
CIPercentage	N/A	Not applicable for the PHI as this feature is not used for the PHI.
id	Algorithm ID under 'details' ID used in the URL (www.evidencio.com/models/show/10531)	The ID is the Evidencio specific identification number of the algorithm.
author	Algorithm author under 'details'	Name of the Evidencio user who created the algorithm on the Evidencio platform.
title	Title of the algorithm (part A of figure 1).	-
variables	Input variables and their entered value. (part N. of figure 1)	The API displays the variables as unique IDs.
min	N/A	Depicts the lowest value when the result of the algorithm is a range. Since the PHI always displays a single value as a result, this value is the same as the 'result'.
max	N/A	Depicts the highest value when the result of the algorithm is a range. Since the PHI always displays a single value as a result, this value is the same as the 'result'.
additionalResultSet	N/A	N/A
mintxt	N/A	Same as 'min', but as a string.
maxtxt	N/A	Same as 'max', but as a string.
result	The main result of the algorithm, the PHI score.	-
resultText	The text displayed in front of the main result	e.g. "The Prostate Health Index (PHI) score is: "
postresultText	The text displayed behind the main result	-
formulaSegments	N/A	-
conditionalResultArray	Result interpretation displayed beneath "Conditional Information" (section O. in figure 1).	The API result shows the raw HTML text that is rendered by the software used for the graphical user interface.
conditionalResultText	Result interpretation displayed beneath "Conditional Information" (section O. in figure 1).	This section is the same as *'conditionalResultArray',* but displayed as a single string.
UDI	Same as the UDI displayed in the GUI (section F. in figure 1).	-
medicalDevice	The electronic label (section I. in figure 1).	The API refers to the electronic label on the graphical user interface.
userManual	The user manual (section K. in figure 1).	The API refers to the location of the user manual at the user interface & Evidencio website).

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. The party performing the integration of the PHI using the API should adhere to the requirements outlined in **10531-DOC-45 Instructions for API integration Prostate Health Index (PHI)**.

11. User manual revision history

Version	Revision notes
V1.0 MAR-2026	Original version

12. Manufacturer details

Contact details of Evidencio:

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