MAMMORISK

MammoRisk® v2.8

Instruction manual

Version 8 (Date May 2025)

MammoRisk

CE

Manufacturer: Predilife, Institut Gustave Roussy,

39 rue Camille Desmoulins,

94805 Villejuif Cedex, France

Modifications history			
Version	Date	Authors	Description
1	05/2018	S.Phung	MammoRisk v2.7.0
2	06/2019	S.Phung	MammoRisk v2.7.1
3	08/2020	S.Phung	MammoRisk v2.7.2 to v2.7.3
4	01/2021	S.Phung	MammoRisk v.2.7.4 to v2.7.5
5	04/2024	S.Phung	MammoRisk v.2.7.6
6	03/2025	B.Dirattana	MammoRisk v2.8
7	15/04/2025	B.Dirattana	MammoRisk v2.8
8	05/2025	B.Dirattana	MammoRisk v2.8

I. Introduction

1. Aim

The aim of this document is to provide a detailed description of how to use the MammoRisk software v.2.8 It is recommended to read the user manual carefully before using the MammoRisk software.

2. Availability of documentation

Electronic version of MammoRisk User Manual is available on Predilife website (www.predilife.com) in PDF format. User may request the manual in paper format by sending an e-mail to support@predilife.com, and Predilife undertakes to supply it within 7 calendar days at the latest.

3. Logotype meaning

The following symbols may be found in product documentation or on the device label:

UDI	Unique device identification	Unique numeric or alphanumeric code linked to a medical device
MD	Medical device	Indicates that the product is a medical device
	Manufacturer's name and address	Manufacturer's name and address
REF	Catalog number	Indicates software reference
SN	Software version number	Indicates software version number
	Electronic operating instructions indicator	Indicates that the user must consult the operating instructions or electronic operating instructions. In the case of electronic operating instructions, the consultation will be indicated next to this symbol
CE	CE marking	The product complies with the requirements of Regulation (EU) 2017/745 on medical devices placed on the market within the European Union.
	Manufacturing date	Indicates the date on which the medical device was manufactured.

	Warning sign	Indicate a safety warning when using the software.

4. Manufacturer and product identification

Product name: MammoRisk

Manufacturer details:

Predilife

39 rue Camille Desmoulins, 94805 Villejuif Cedex, France (Headquarters)

343 Bureaux de la colline, 92210 Saint Cloud, France (Operational site)

SRN: FR-MF-000001863

BASIC UDI: 37011265000Predirisk6D

5. Scope of the software

The MammoRisk software, designed to be quick and easy to use in routine practice, provides healthcare professionals with information on women's breast cancer risk profile in order to enable users to personalize prevention, adapt screening strategies and encourage early detection of the disease.

The MammoRisk software calculates the probability of breast cancer occurrence for women from the general population or not.

The MammoRisk software does not constitute an aid to interpretation or diagnosis.

a. Intended use

The MammoRisk software is designed to provide information on women's breast cancer risk profiles to support healthcare professionals in their patients' follow-up.

MammoRisk does not constitute an aid to interpretation or diagnosis, it provides additional information to enable healthcare professionals to adapt the screening examinations for each patient.

b. Intended users

Users of MammoRisk software are limited to healthcare professionals with medical knowledge regarding breast cancer; to help them communicate and discuss breast cancer risk with their patients.

c. Intended Target population

The target population is women, who are asymptomatic of breast cancer.

6. Residual risks

The intended use of the MammoRisk software does not present any residual risks related to the device for its direct user (healthcare professional) or for the patient. However, some residual risks associated with its use are mentioned below, along with recommendations.

a. Limitation

MammoRisk is a software to calculate a risk score prediction for breast cancer and not a diagnostic tool.

It provides additional information to help the healthcare professional assess the risk of breast cancer and adapt screening examinations for each patient.

b. Contraindication

MammoRisk is a software that does not expose the user or the patient to any immediate danger: it can be used as often and for as long as necessary, at any time and with any setting set by the user.

The following patients are not eligible for MammoRisk software:

- women with symptom of breast cancer

The following patients are not eligible for general population score:

- women with a personal history of breast cancer,
- women with a personal history of ovarian cancer,
- women who have undergone thoracic radiation,
- women with a previous biopsy showing high-risk lesions on the breast,

- women under 40 years-old and over 74 years-old
- women with a significant family history, including family history of BRCA1 or BRCA2 mutation, one or more family histories of breast cancer in one or more women under the age of 40, two or more first-degree relatives with a history of breast or ovarian cancer, a family history of breast cancer in men

Among patients with significant family history, the following patients are not eligible for the Tyrer-Cuzick score:

- women with a personal history of breast cancer,
- women who have undergone thoracic radiation,
- women with a previous biopsy showing high-risk lesions on the breast,
- women over 85 years-old

The following patients are not eligible for Eisinger score:

- women outside of France

c. Warning

The software is to be used only by healthcare professionals with scientific training and medical knowledge in breast cancer and prevention.

The software could underestimate the real risk of certain patients, which could influence medical recommendations and deprive some women of enhanced screening.

The data or information provided by the software should not be considered as recommendations for the patient; it is the sole responsibility of the healthcare professional(s) to make personalized recommendations to their patients.

The software is a risk assessment tool and should never be used as a substitute for a medical consultation or diagnosis by a healthcare professional.

Although the assessment risk is accurate, it is a statistical calculation based on algorithmic processing and cannot accurately determine the likelihood that a woman will develop breast cancer.

MammoRisk test results should be interpreted by a healthcare professional in the context of the patient's complete clinical and family history. Decisions regarding breast cancer screening and prevention practices should not be based solely on a patient's MammoRisk results.

d. Precaution

Healthcare professionals using MammoRisk must undergo specific training to ensure proper use of the software and correct interpretation of results.

It's essential to make it clear to patients that the score provided is not a diagnosis, but a calculation of risk that can be used to tailor follow-up.

e. Side effects

There are no side effects to report, as MammoRisk is predictive software that calculates a risk score for developing breast cancer.

f. Adverse events

On the market since 2018, no adverse events have been reported. MammoRisk is a predictive software that calculates a risk score for developing breast cancer.

7. Cybersecurity residual risks

MammoRisk has been developed according to validated and compliant processes, deployed on servers designed to host e-health applications, and uses standardized and secured communication protocols. Despite these security measures, certain vulnerabilities may still exist, depending on the environment in which the software is used and the evolution of threats. The user is encouraged to read the warnings, precautions and limitations in the following paragraphs.

In case of any cybersecurity concerns or suspected security breaches, the user shall reach out to the support team without delay (see Contact section).

a. Limitation

While MammoRisk incorporates robust security measures, certain technical and operational constraints exist. For example, the software:

- Requires an active internet connection for data synchronization and does not support offline use;
- Is intended for use only on authorized, secure devices; it has not been tested on jailbroken or rooted devices;
- Follows industry-standard protocols but is not designed to detect or prevent every type of cyberattack.

Users should implement supplementary security measures such as firewalls, intrusion detection systems, and regular system audits to further protect the system.

b. Warning

MammoRisk shall not be installed on operating systems or platforms that do not meet the minimum-security requirements, as this may expose the device to unmitigated risks. Additionally:

- The use of the software in environments lacking proper IT security (e.g., absence of a firewall, antivirus, or regular update procedures) is strongly discouraged;
- Disabling, modifying, or bypassing built-in security features (such as password authentication, automatic logout, and multi-factor authentication) is strictly prohibited, as doing so increases the risk of unauthorized access and system compromise;
- Users must remain alert to any abnormal behaviors such as unexpected pop-ups, sluggish performance, suspicious network activity, or unusual error messages and report them immediately to the support team (see Contact section).

c. Precaution

To minimize cybersecurity risks, users shall take the following precautions:

- Ensure that operating system and network security settings (firewalls, antivirus software, malware detection tools) are configured according to best practices, including timely updates for both the operating system and critical applications;
- Confirm that their device is connected to the designated secure network (verify the URL uses HTTPS) before logging in;
- Use strong, complex passwords and keep credentials confidential;
- Follow established protocols, including regular data backups and restoration procedures, to ensure business continuity;
- Only trained and authorized personnel should access the system. Promptly contact technical support if any issues, such as login errors or suspected breaches, are encountered (see Contact section).

8. Claim regarding the safety

MammoRisk is a software that does not expose the user nor the patient to any immediate danger: it can be used as often and for as long as necessary, at any time and with any setting set by the user.

In view of the study of the scientific literature concerning the use of risk scores, there is no report of vigilance concerning the safety of the use of these scores in the populations studied.

9. Claim regarding the performance

The use of MammoRisk software allows healthcare professionals to stratify women according to their risk of breast cancer.

The risk models used in the MammoRisk software accurately calculate an absolute individual 5-year breast cancer risk score for a woman belonging to the general population (general population score) or not (Tyrer-Cuzick score).

The MammoRisk software enables healthcare professionals to assess the relevance of a genetic counseling to search for a genetic alteration using the Eisinger family tree analysis score.

10. CE marking

The MammoRisk software, developed by Predilife, obtained the CE marking in 2018 (class I medical device) under medical device directive 93/42/CEE.

The MammoRisk software was developed in accordance with the EN 62304/A1:2018 standard, which defines lifecycle processes for medical device software.
Verification and validation activities were conducted according to Predilife's internal software testing procedures to ensure that the software meets its specified requirements. A risk analysis has been performed in compliance with EN ISO 14971.

11. User training

Users of the MammoRisk software must have undergone training. If this training course has not been given to the user of the software, please contact the support team (see the Contact section).

12. Labelling

The label contains:

- The UDI version and the associated pictogram,
- The Medical Device pictogram,
- The catalog number and the associated pictogram,
- The software version number and the associated pictogram,
- The manufacturing date and the associated pictogram,
- The manufacturer's name and address and the associated pictogram,
- The link to the user manual and the associated pictogram,
- The CE marking pictogram and the associated pictogram with the reference number of the notified body.

13. Incident reporting

Any serious incident occurring in connection with the medical device must be notified to the vigilance correspondent of Predilife at the following e-mail address: quality@predilife.com and to the local competent authority.

II. Software initial setup

1. Environment of use, including compatible browsers

The software operates as a cloud-based SaaS solution. To use the application and access its user interface on a workstation, please ensure that the environment meets the following requirements:

- Operating System: The workstation must be running Windows 10 or later, or macOS version 11 or higher.
- Web Browser: An up-to-date web browser is required. The following browsers are supported:
  - Mozilla Firefox version 96 or higher
  - Google Chrome version 107 or higher
  - Microsoft Edge version 107 or higher
  - Apple Safari 16 or higher
- Network Requirements: A stable and secure Internet connection is recommended to ensure optimal performance and access to the latest updates.

These specifications ensure that the software operates reliably in a secure and compatible environment. For further inquiries regarding system compatibility or additional technical requirements, please contact the support team (see Contact section).

2. Configuration of security features (CNFS)

   MammoRisk being a cloud-based SaaS solution, all security features are pre-configured and managed on the server side. There is no need to manually adjust any security settings. The system automatically employs industry standard security measures such as HTTPS, secure authentication, and data encryption to protect the data.

3. 3rd party software

   To use MammoRisk effectively, it is essential that certain third-party software components are installed and meet specified criteria. The users must access the application via a supported web browser that adheres to the security and compatibility standards. In addition, the operating system and antivirus software on the workstation must be maintained and kept up to date. Please refer to the dedicated section for minimal versions of browsers and operating systems.

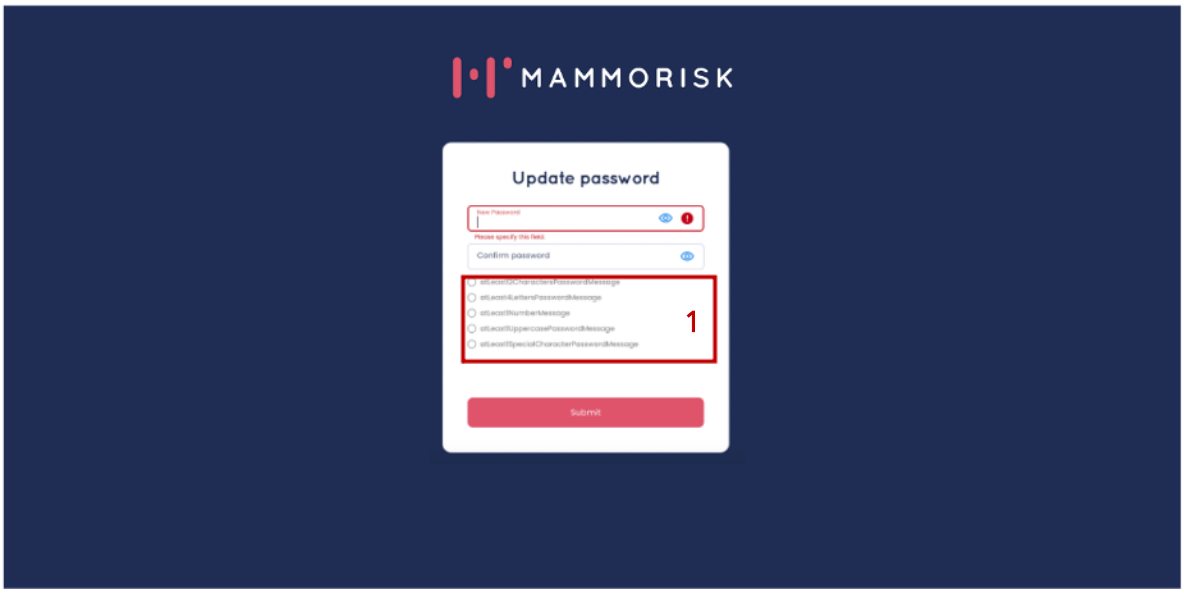
   MammoRisk can also be used via API only. To integrate with the API, please refer to the integration documentation, which is available upon request from the support team (see Contact section).

   It is the responsibility of the user to ensure that these third-party components are properly configured and regularly updated. This includes implementing supplementary security measures such as firewall rules (please allow port 443 and URL mammorisk.predilife.com in white list), robust authentication protocols, network segmentation, and endpoint protections. Together, these measures help safeguard the overall IT environment and ensure secure, reliable access to MammoRisk.

   Should any cybersecurity concerns or compatibility issues with third-party software arise, please contact the support team immediately (see Contact section).

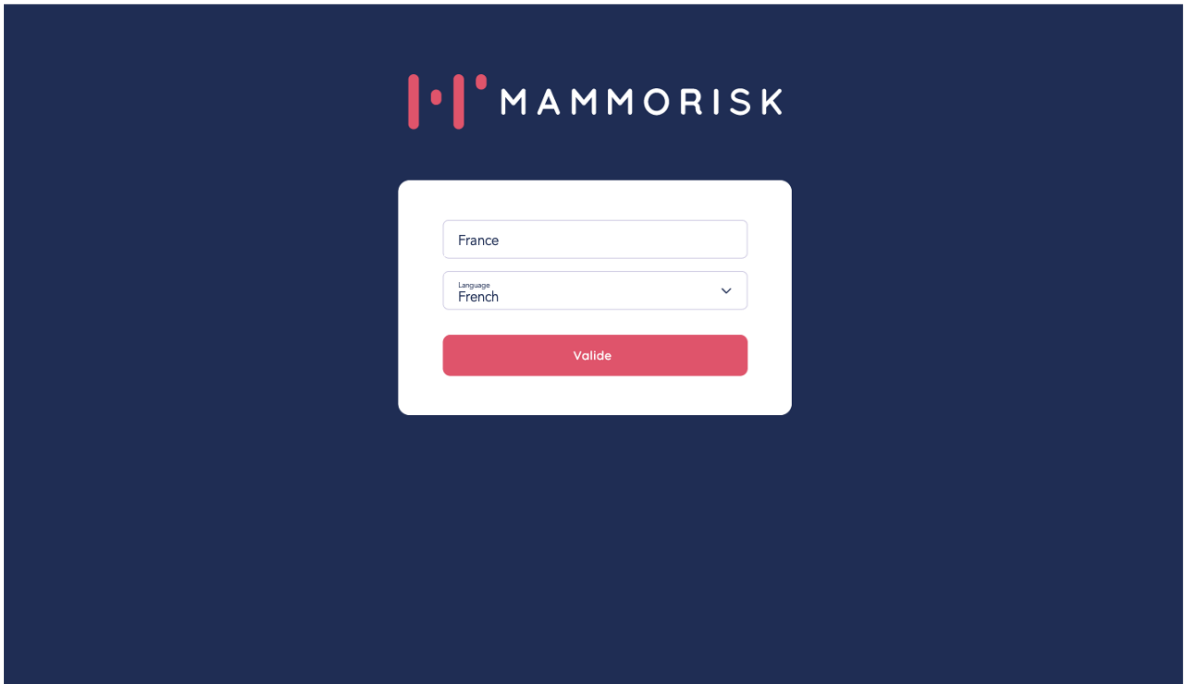
4. Start a new session

   The user account is created by the technical team, and upon first login, the user will be prompted to set their own secured password. The password must comply with the rules indicated (1) and must not be shared.



Once the password has been set, the user must define the language of their space.

The languages offered depend on the configuration made when the account was created.

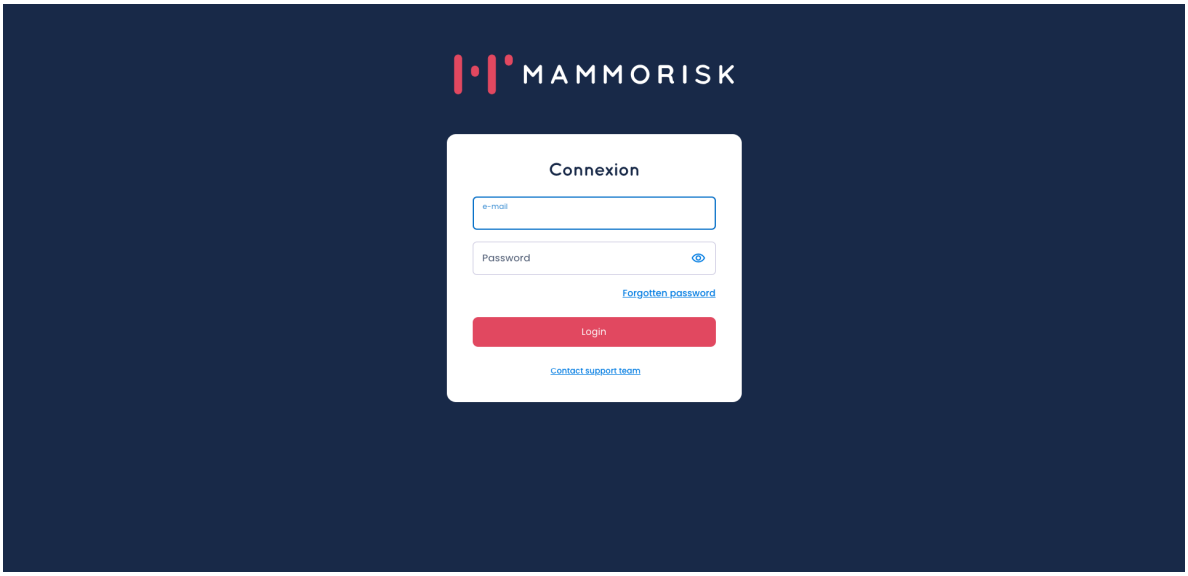


Once the language has been set, the user must accept the general conditions of use by checking the box (1). Once the conditions have been accepted, the user will be able to create patient files and examinations.

III. MammoRisk software

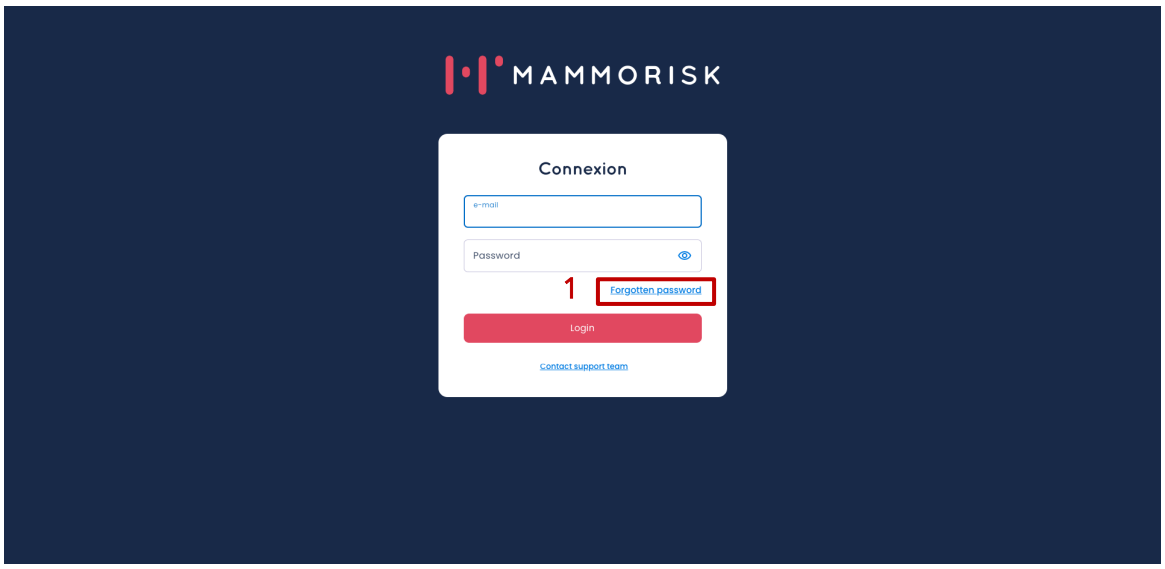
1. Login

To connect to the MammoRisk software, users must access their healthcare professional's area by entering their login and password.

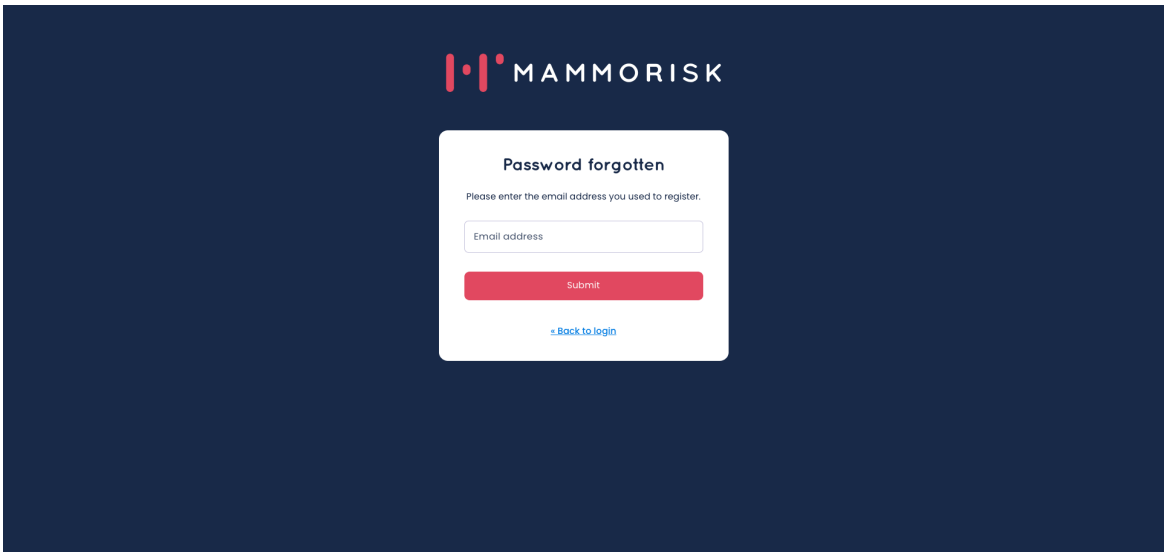


2. Password reset

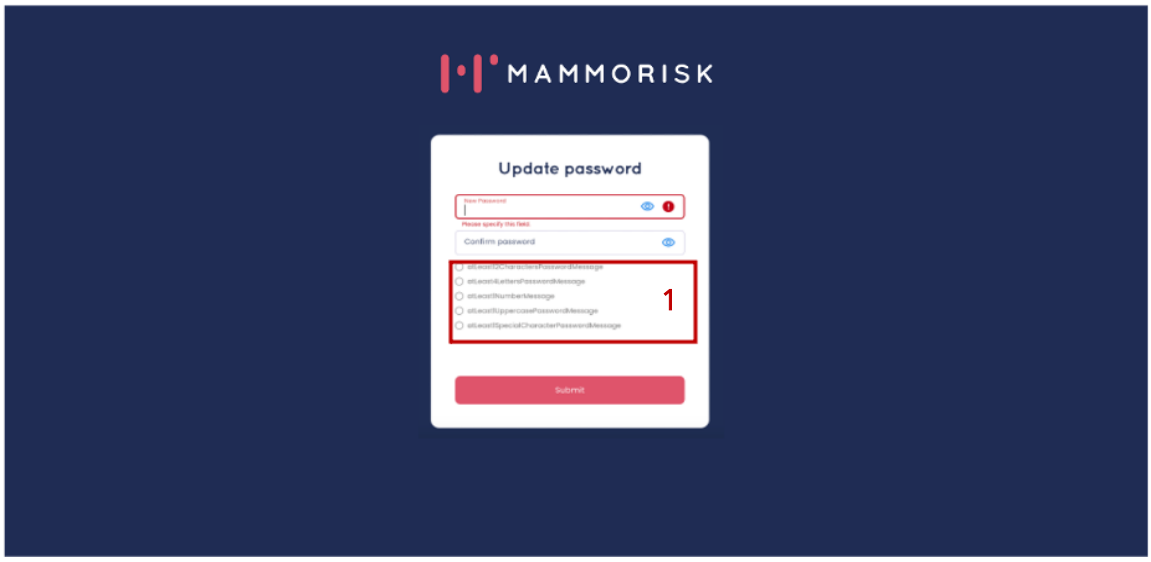
If the user doesn't remember their password, it can be reset by clicking on “Forgotten password” (1).



The user will then need to enter their e-mail address to receive the password modification link.



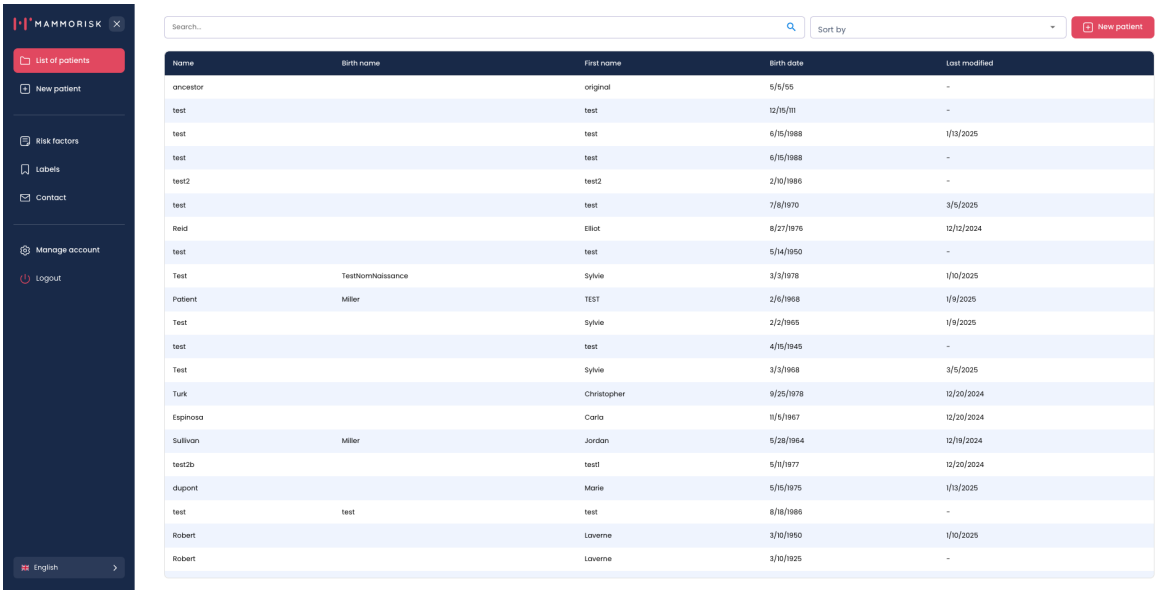
Once the user has clicked on the link, they will be prompted to reset their password according to the rules indicated (1), which must be different from the previous password.



3. Patient's index

On the main screen, the user can consult the list of all patient files created by the healthcare professional. It contains the following information: the patient's identification data (surname, birth name, first name, date of birth) as well as the date of last update of the file.

In a center bringing together several healthcare professionals, each of them will also have access to the files of patients followed by their colleagues.

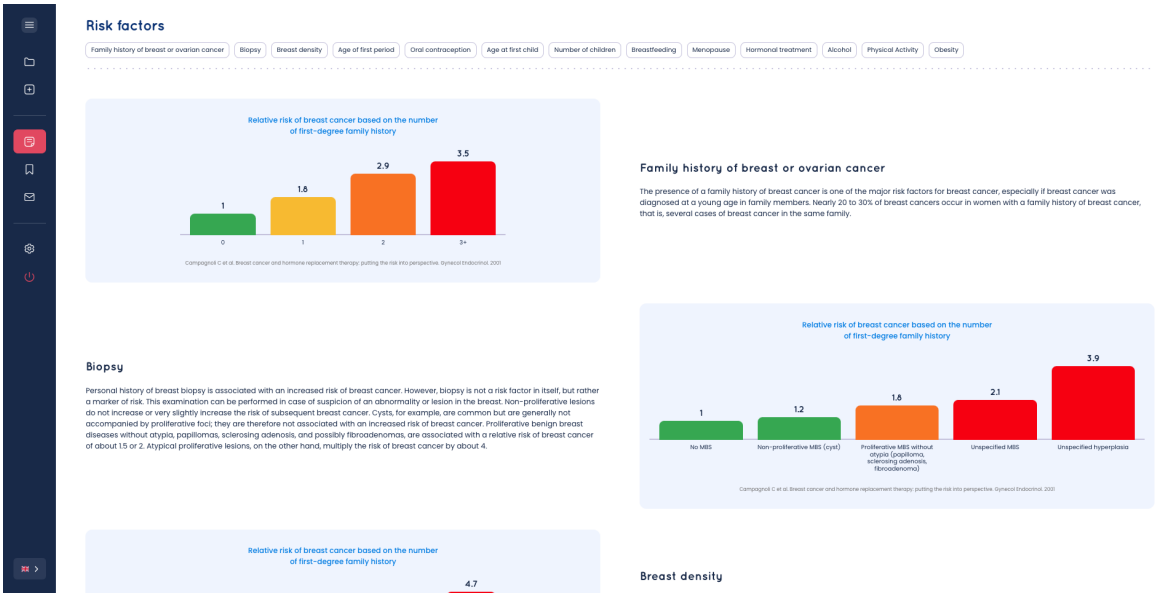


4. "Risk factors" tab

The "Risk factors" tab allows the user to access information relating to all the risk factors taken into account by the software, as well as those recognized for their influence on the occurrence of breast cancer.

This information is presented in the following form:

- The risk factor concerned, accompanied by an explanation of its meaning as well as its impact on the risk of breast cancer (positive or negative).
- A graph illustrating the evolution of the relative risk according to this factor.



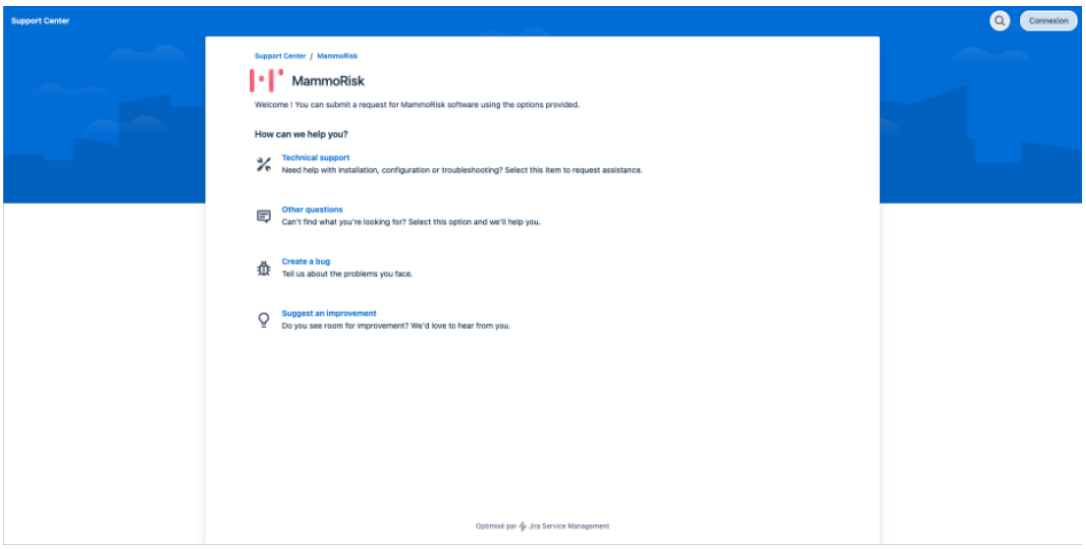
5. "Label" tab

The "label" tab allows the user to access the regulatory label (see labelling section) and the user manual.

6. "Contact" tab

The "Contact" tab allows the user to report a problem encountered with the software by sending a message to the Support team. By clicking on this tab, the healthcare professional is redirected to a complaint and error reporting form, where they must complete the required fields before clicking on the "Send" button.

For any configuration request, the user can also use the form or contact the Predilife team at the following address: support@predilife.com.



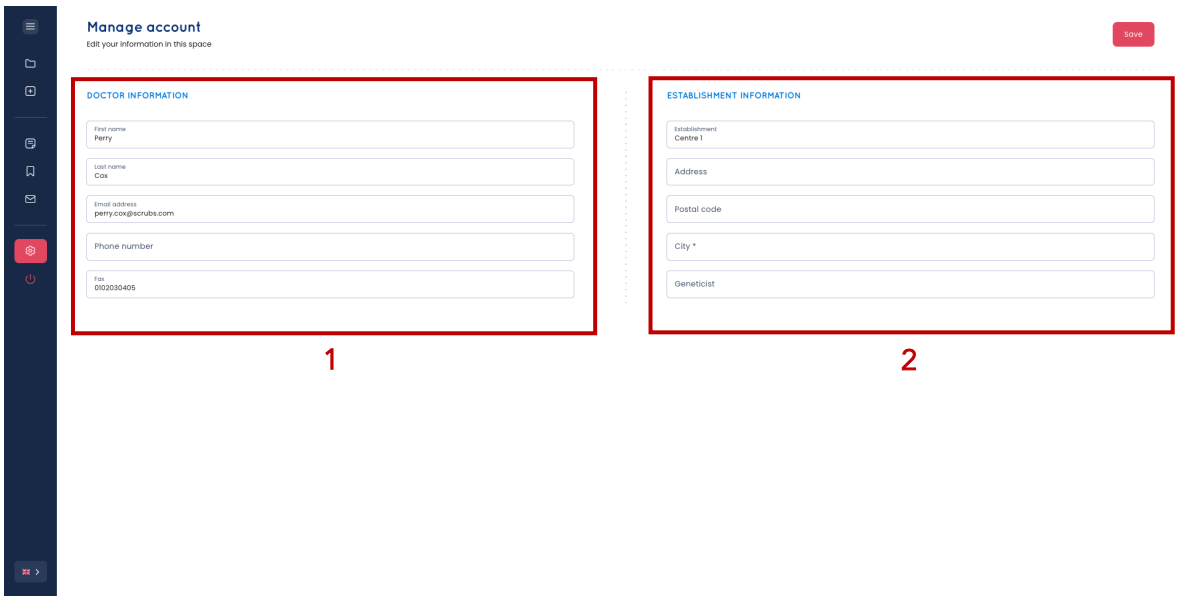
7. "Manage account" tab

The "Manage Account" tab allows the user to update their personal information (1). After making the desired changes, they must click on "Save" to save them.

The modifiable information is as follows:

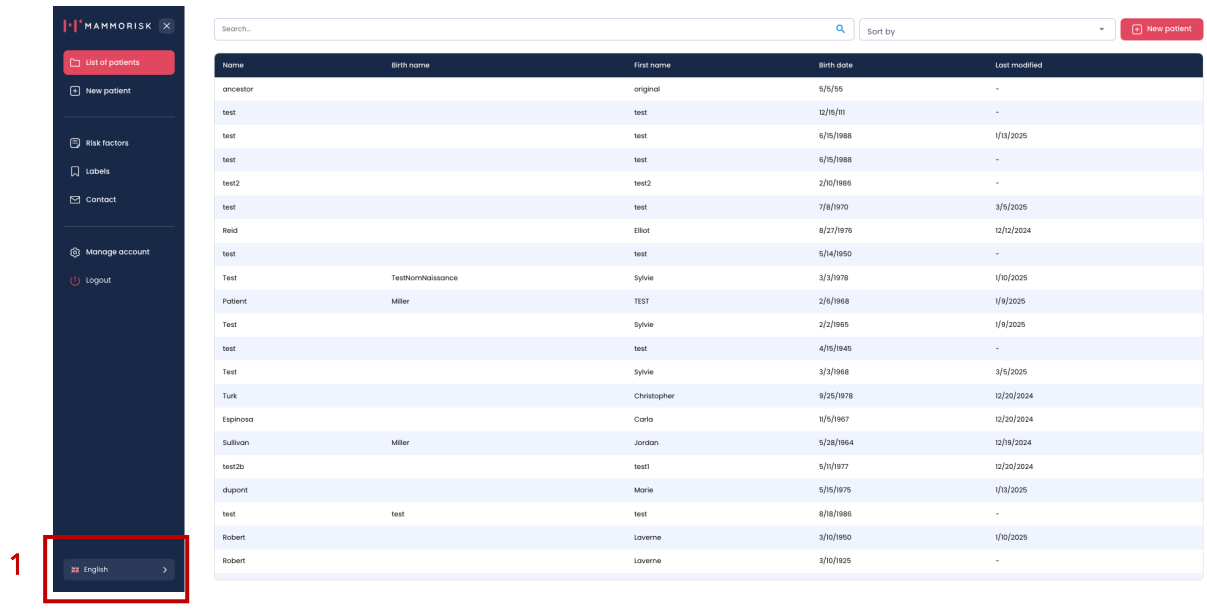
- First name
- Name
- Email address
- Phone number
- Fax number

On the other hand, information linked to the establishment to which the healthcare professional is attached cannot be modified (2).



8. Languages

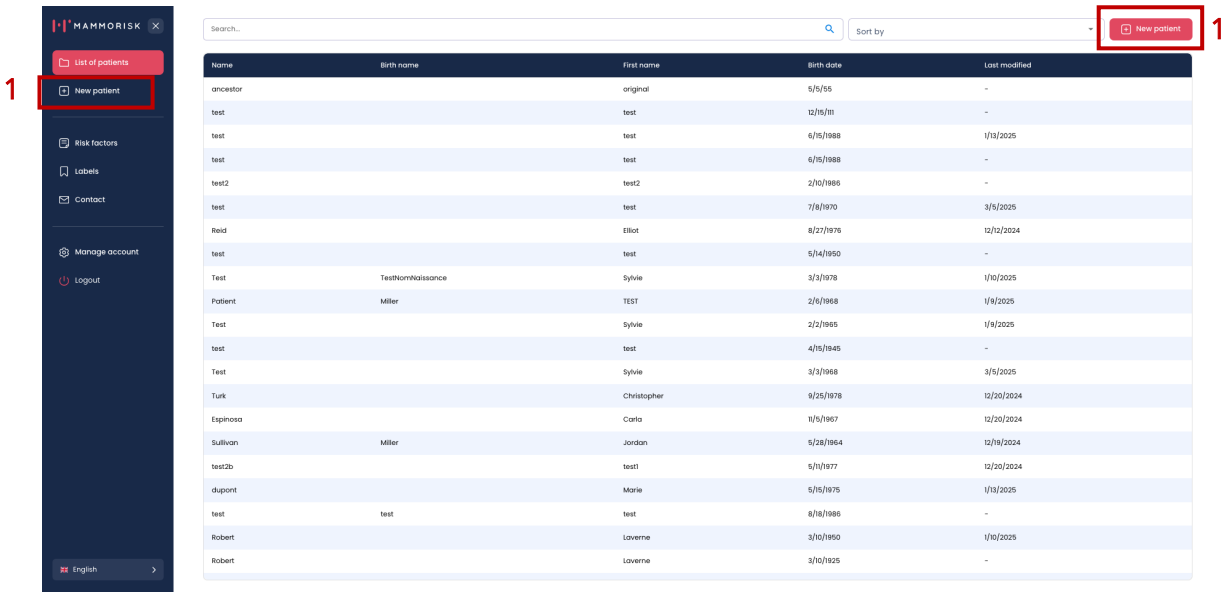
The user can change the language of their interface by clicking on the button located at the bottom left (1). The accessible languages are those defined during initial account setup.



IV. Patient file management

1. Creation of a patient records

The user can create a new file for a patient in order to calculate her risk score by clicking on the button **"New patient"** (1).



They must then fill in the various mandatory fields, indicated by an asterisk (1). In the case of hospitals or clinics, an identification number can be added, although this information remains optional.

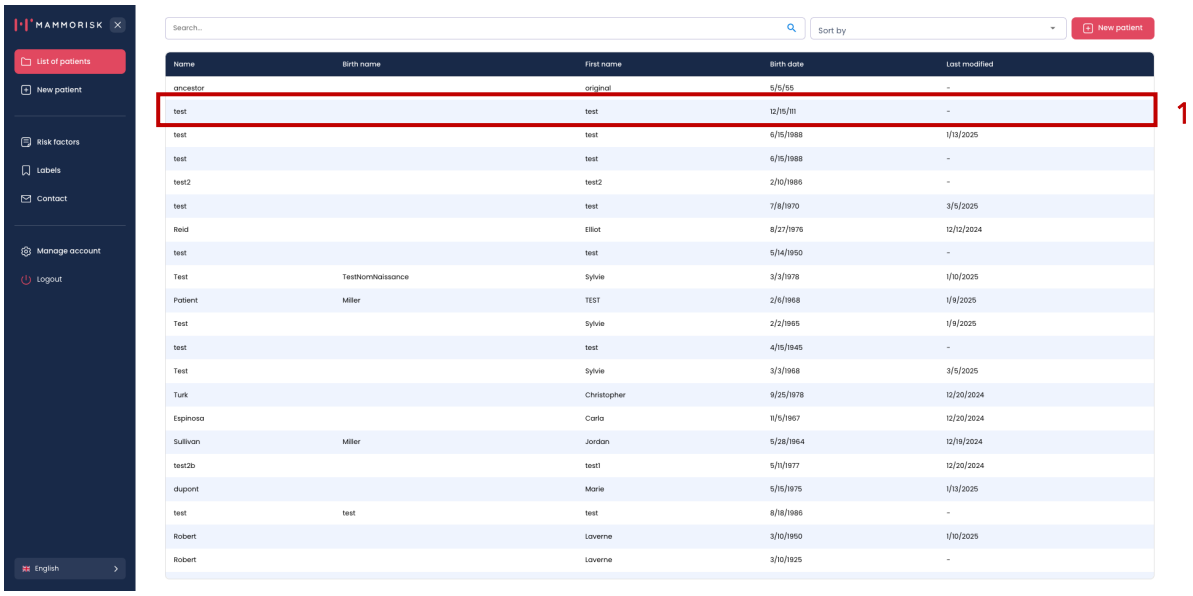
Once all mandatory fields have been completed, two options are available to the user:

- " **Save and quit** ": the patient's file is created and the user is redirected to the patient file index (2).
- " **Access the questionnaire** ": the user continues the risk assessment by being redirected to the preliminary questionnaire (3).

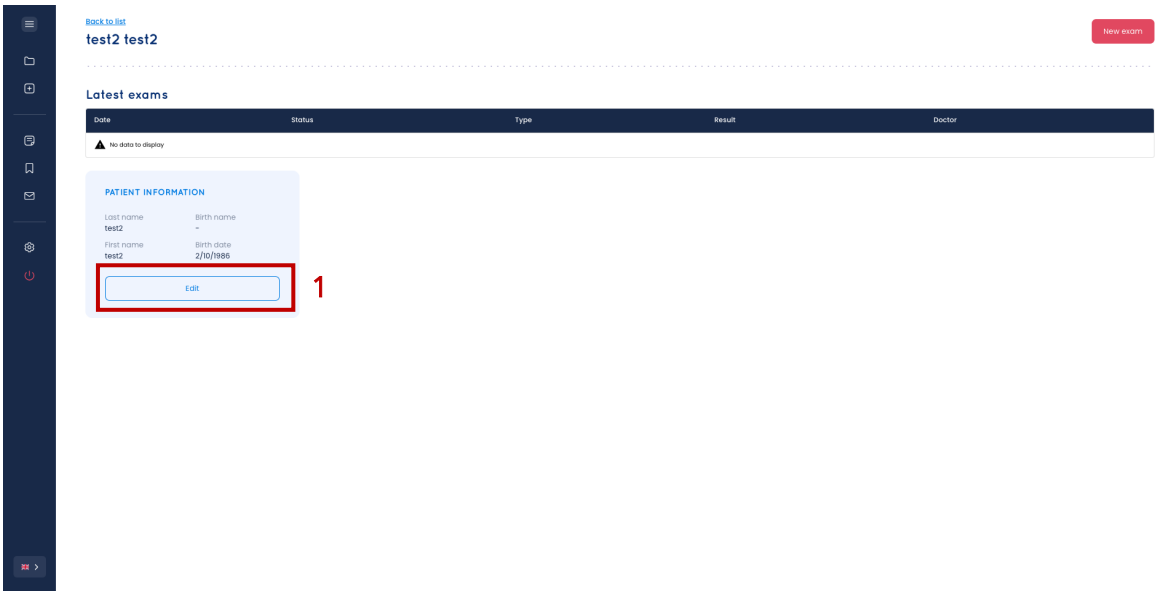
2. Editing a patient record

The user can modify the information in a patient's file in the event of an entry error or to add missing information.

To do this, they must select the patient's file by clicking on it (1), which will allow them to access the information and make the necessary modifications.



Once the file is selected, the healthcare professional must click on the button **« Edit »** located in the insert **Patient information**, under the list of exams (1). This will allow them to edit the information in the file and correct or add data if necessary.



Once in edit mode, the user will be able to access the different fields containing the information entered when creating the file. They can then modify the desired fields according to his needs (1).

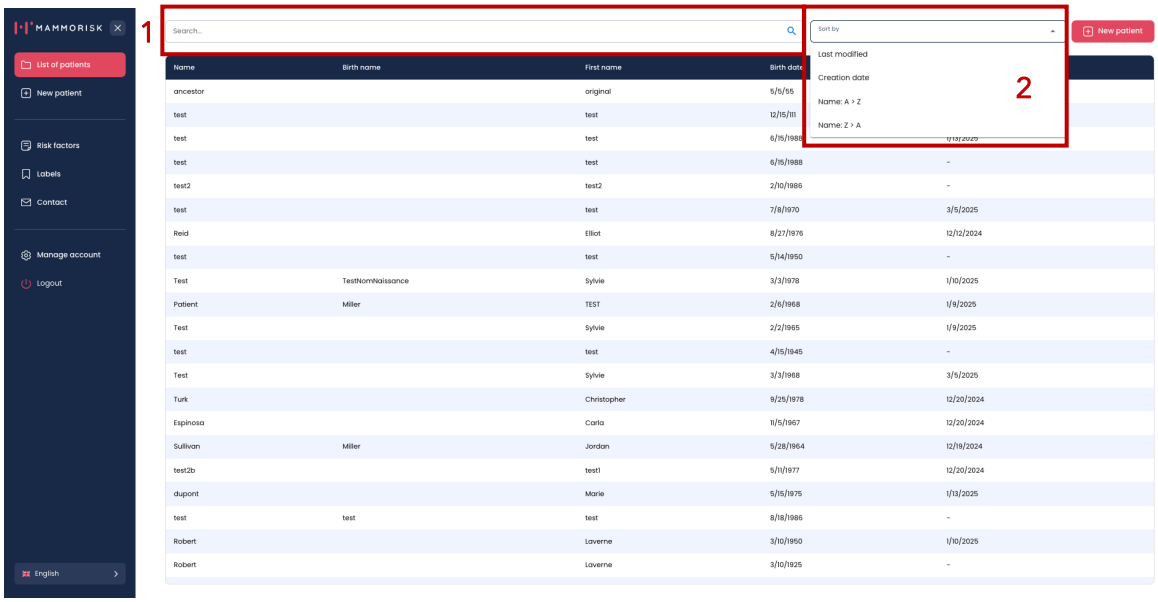
Once the modifications have been made, two options are available to them:

- « **Save and quit** »: the modifications are saved and the user is redirected to the patient file index (2).
- « **Access the questionnaire** »: the modified information is saved and the user is redirected to the preliminary questionnaire to continue the risk assessment (3).

3. Patient records filters

The user can apply filters to search a patient's file. Two options are available to them:

- Search by name: by entering the patient's name in the search bar (1).
- Folder filtering: by applying sorting criteria to the folder index. The sorting options are (2):
    - Alphabetical order
    - Reverse alphabetical order
    - Creation date (newest to oldest)
    - Date last modified (newest to oldest)

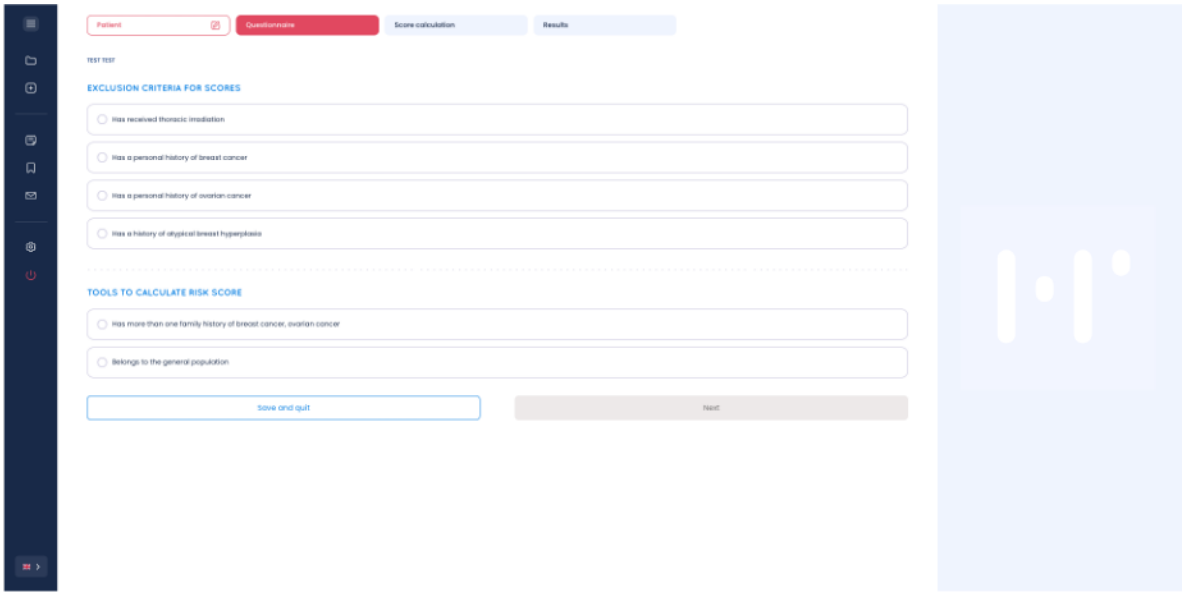


V. Exam management

1. Creating an exam

The user can create a new exam for a patient to calculate her risk score by clicking on the button **"New exam"** (1).

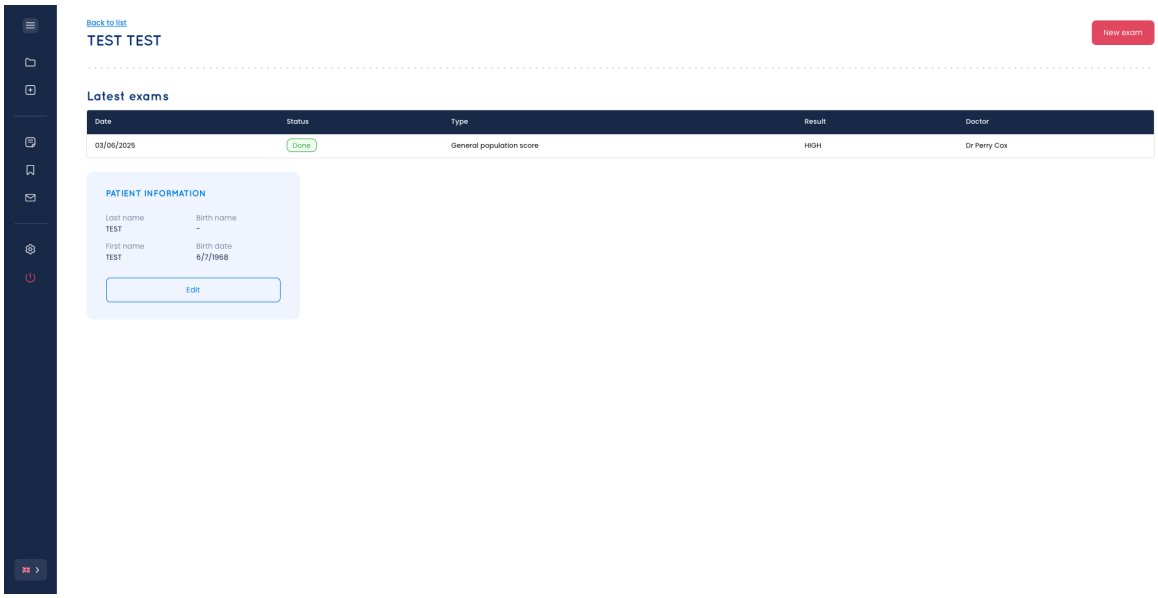
The user is redirected to the preliminary questionnaire to begin assessing the patient's risk.



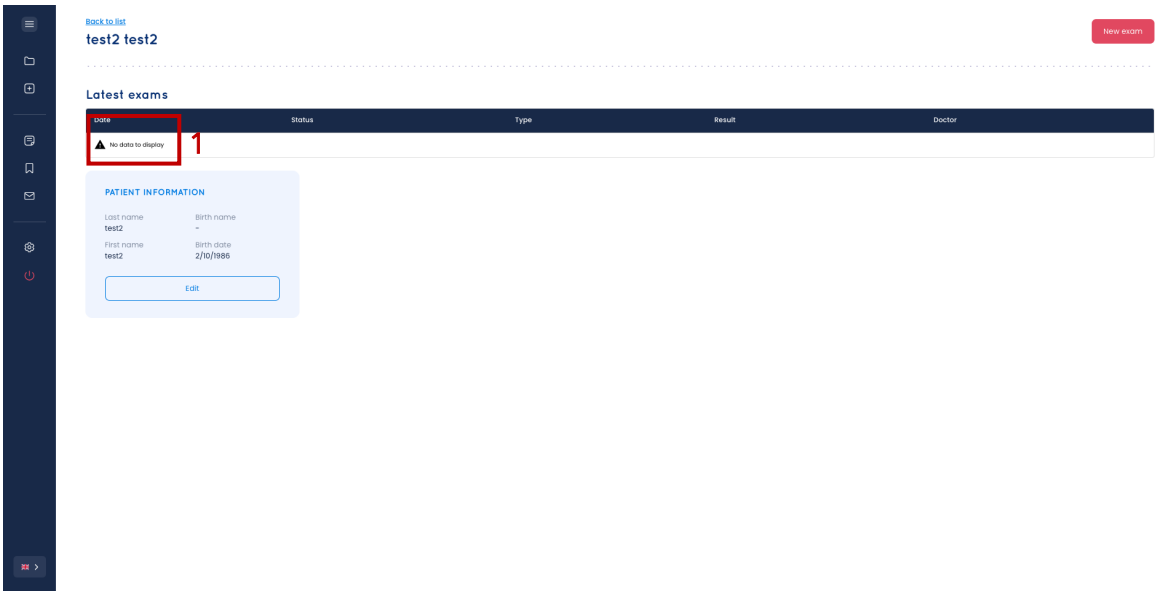
2. Viewing exams

When the user accesses a patient's file, they will be able to consult the examinations associated with this file. The following information will be available:

- Exam date
- Exam Status (In Progress or Completed)
- Type of score used for risk assessment
- Score result, if calculated
- Name of the healthcare professional who calculated the risk score



If the patient has never benefited from a risk assessment, the list of examinations will be empty. In this case, a message **"No data to display"** (1) will be displayed on the screen to inform the user (see figure below).



3. Loading an exam

The user can add a new examination to a patient's file. To do this, they must:

- Select the patient's file by clicking on it.
- Then open the desired exam by selecting it (1).

Depending on the status of the exam, several situations may arise for the user:

- Examination with status "**In progress**": the user is redirected to where they left off the last time they used the software. If information has already been entered in a patient examination file, it will be visible and accessible for modification or addition.
- Examination with status "**Finished**": the user is redirected to the patient's examination file. They will be able to consult the calculated score and the associated recommendations.

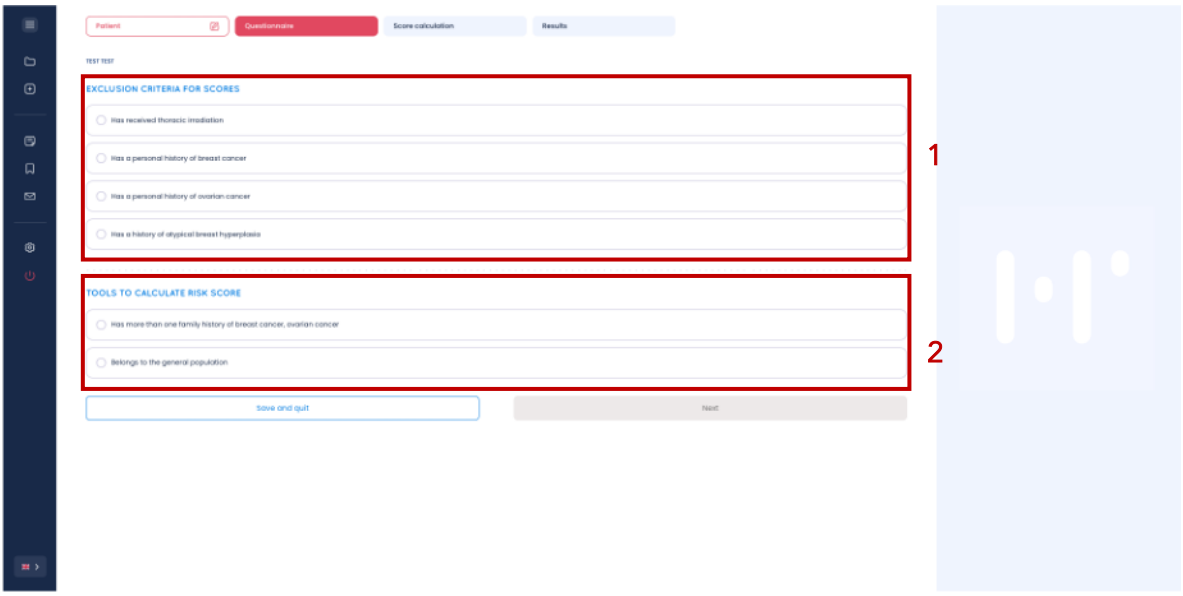
VI. Preliminary questionnaire

1. Presentation

The preliminary questionnaire allows the user to check whether the patient has any personal history that could constitute an exclusion criterion for the use of risk scores (1). In the absence of such criteria, the healthcare professional will be able to select the scoring tool most appropriate to the patient's profile (2).

Patients with a personal history of breast cancer, who have undergone thoracic radiotherapy, or who have atypical breast hyperplasia are classified into a specific risk category (high or very high). In this case, appropriate follow-up recommendations are defined by the healthcare professional.

The user can use the MammoRisk indications diagram to check the patient's pathway using the MammoRisk software (see Appendix 2: MammoRisk indications diagram).

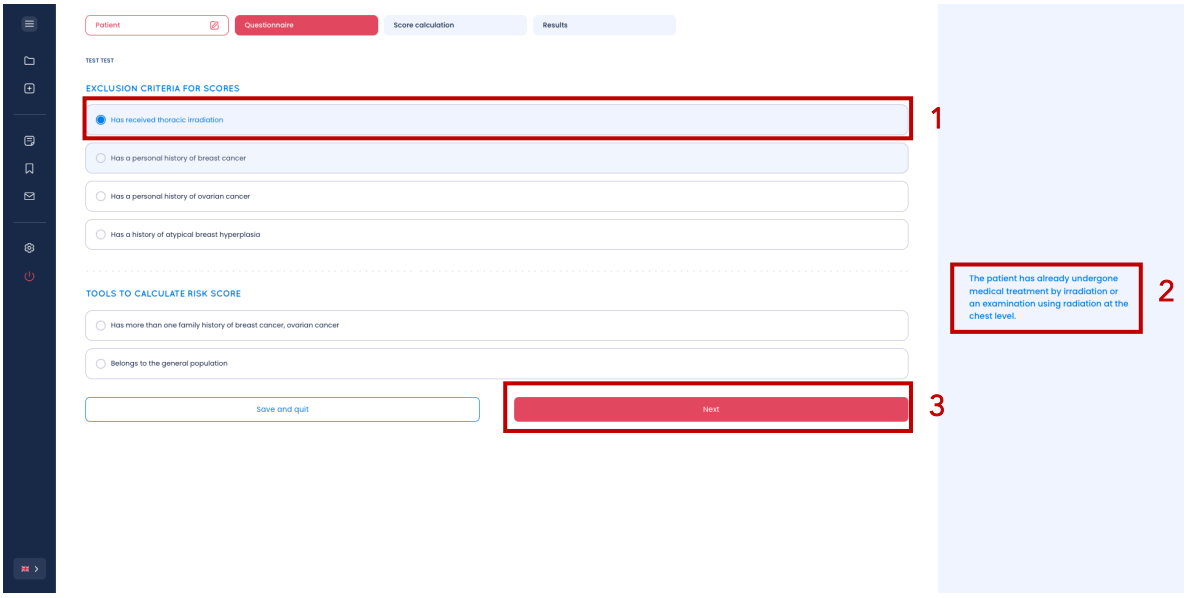


2. Chest irradiation case

a. Presentation

If the patient has already undergone medical treatment by irradiation, the user will check the box “Received chest irradiation” (1). An explanatory sentence will then appear to ensure that the patient meets this criterion (2).

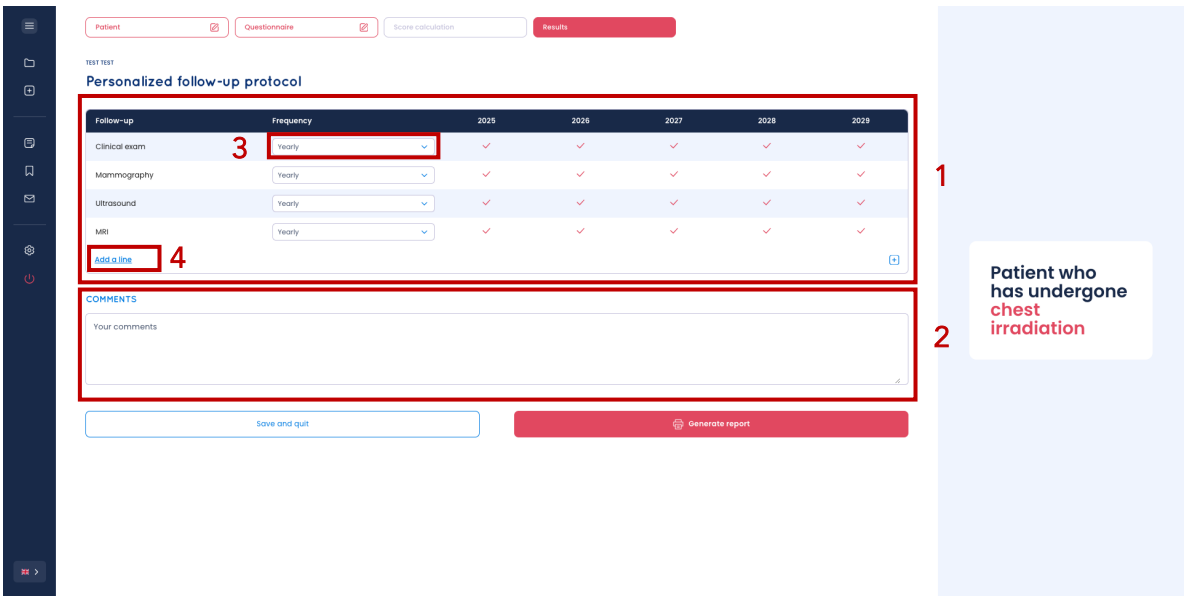
If this is the case, they can click on the “Next” button (3).



b. Recommendations

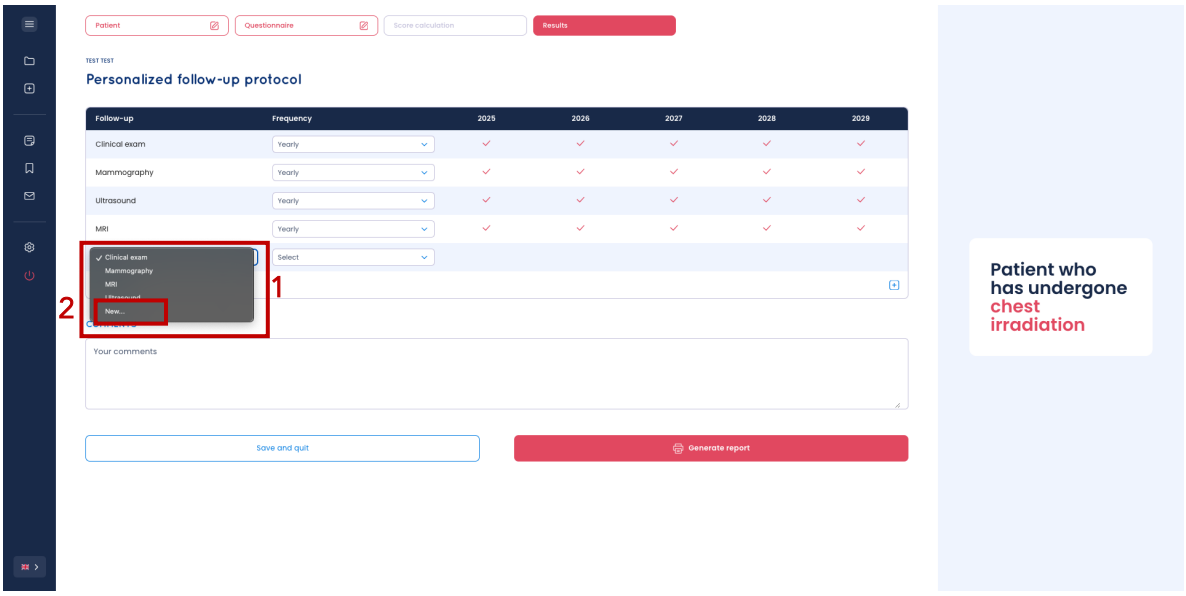
The user will access the recommendations in order to define the personalized patient monitoring protocol. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a “Comments” field to add other recommendations or remarks on the patient’s profile.

They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account. The user can set the frequency of examinations (3) and add more by clicking on “Add a line” (4).

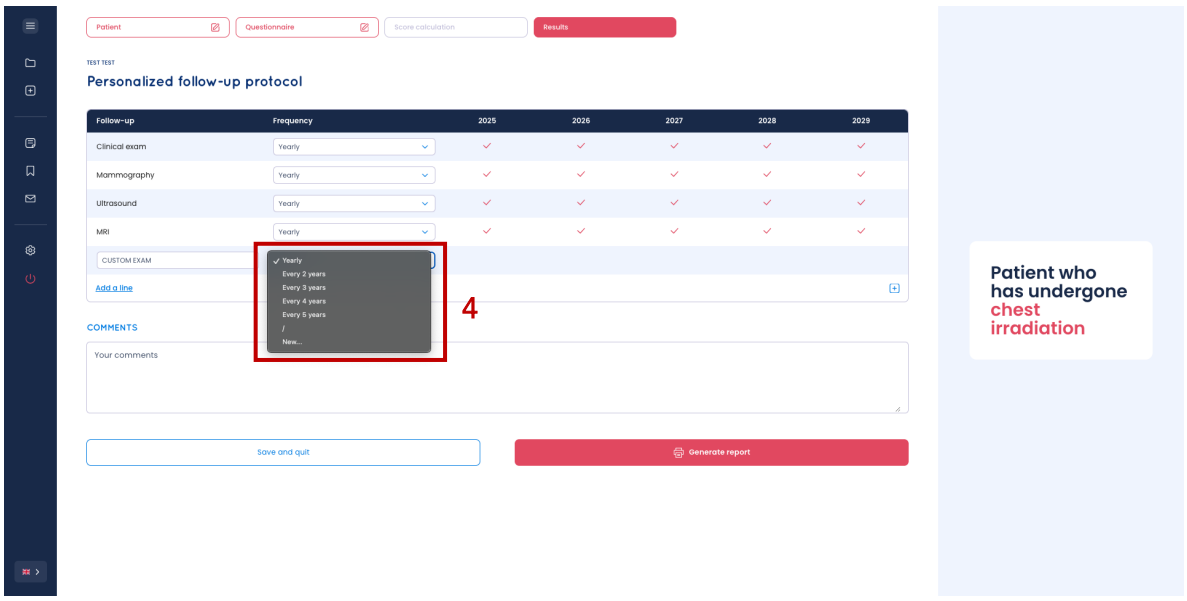


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If they wish to add an exam that is not present in the list, they can select “New” (2) and manually enter the name of the exam.



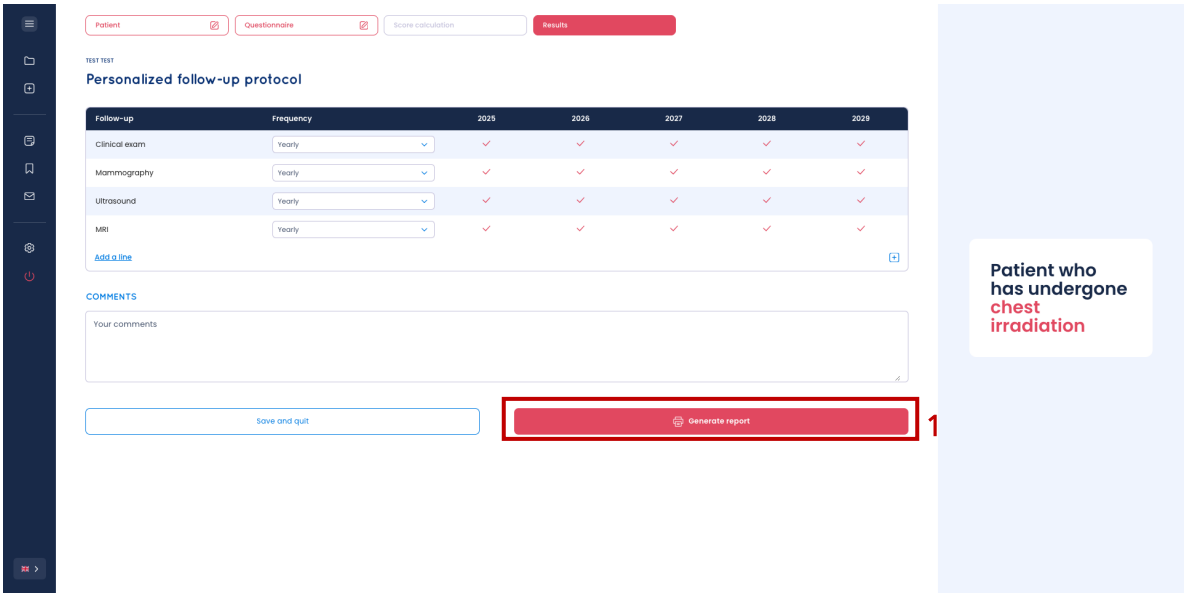
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.

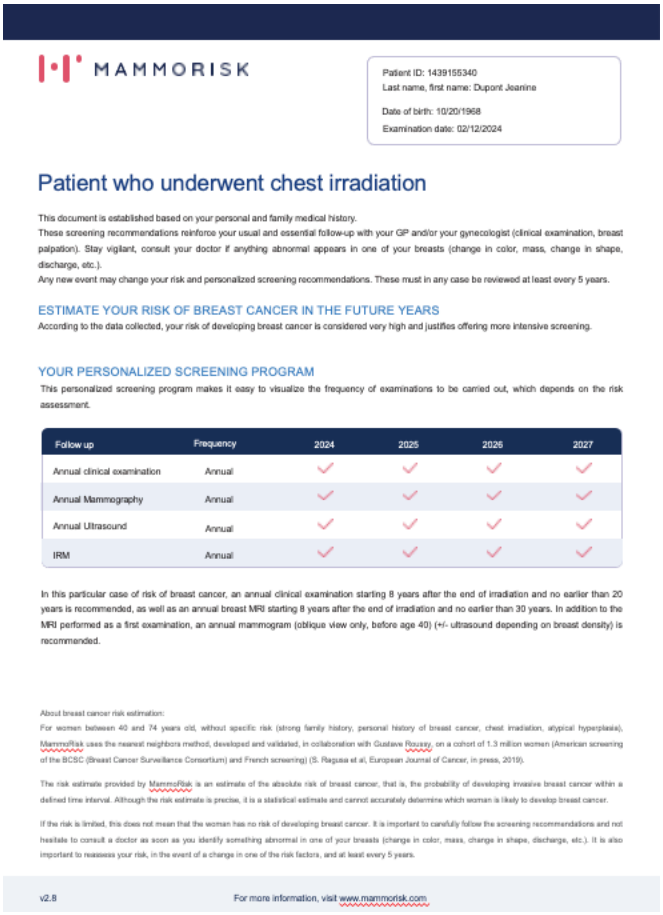


c. Generating a report

Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the "Generate report" button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional's comments.





MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine
Date of birth: 10/20/1968
Examination date: 02/12/2024

Patient who underwent chest irradiation

This document is established based on your personal and family medical history.
These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in any case be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS

According to the data collected, your risk of developing breast cancer is considered very high and justifies offering more intensive screening.

YOUR PERSONALIZED SCREENING PROGRAM

This personalized screening program makes it easy to visualize the frequency of examinations to be carried out, which depends on the risk assessment.

Follow up	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓
IRM	Annual	✓	✓	✓	✓

In this particular case of risk of breast cancer, an annual clinical examination starting 8 years after the end of irradiation and no earlier than 20 years is recommended, as well as an annual breast MRI starting 8 years after the end of irradiation and no earlier than 30 years. In addition to the MRI performed as a first examination, an annual mammogram (oblique view only, before age 40) (+/- ultrasound depending on breast density) is recommended.

About breast cancer risk estimation:
For women between 40 and 74 years old, without specific risk (strong family history, personal history of breast cancer, chest irradiation, atypical hyperplasia), MammoRisk uses the nearest neighbors method, developed and validated, in collaboration with Gustave Roussy, on a cohort of 1.3 million women (American screening of the BCSC (Breast Cancer Surveillance Consortium) and French screening) (S. Ragusa et al, European Journal of Cancer, in press, 2019).

The risk estimate provided by MammoRisk is an estimate of the absolute risk of breast cancer, that is, the probability of developing invasive breast cancer within a defined time interval. Although the risk estimate is precise, it is a statistical estimate and cannot accurately determine which woman is likely to develop breast cancer.

If the risk is limited, this does not mean that the woman has no risk of developing breast cancer. It is important to carefully follow the screening recommendations and not hesitate to consult a doctor as soon as you identify something abnormal in one of your breasts (change in color, mass, change in shape, discharge, etc.). It is also important to reassess your risk, in the event of a change in one of the risk factors, and at least every 5 years.

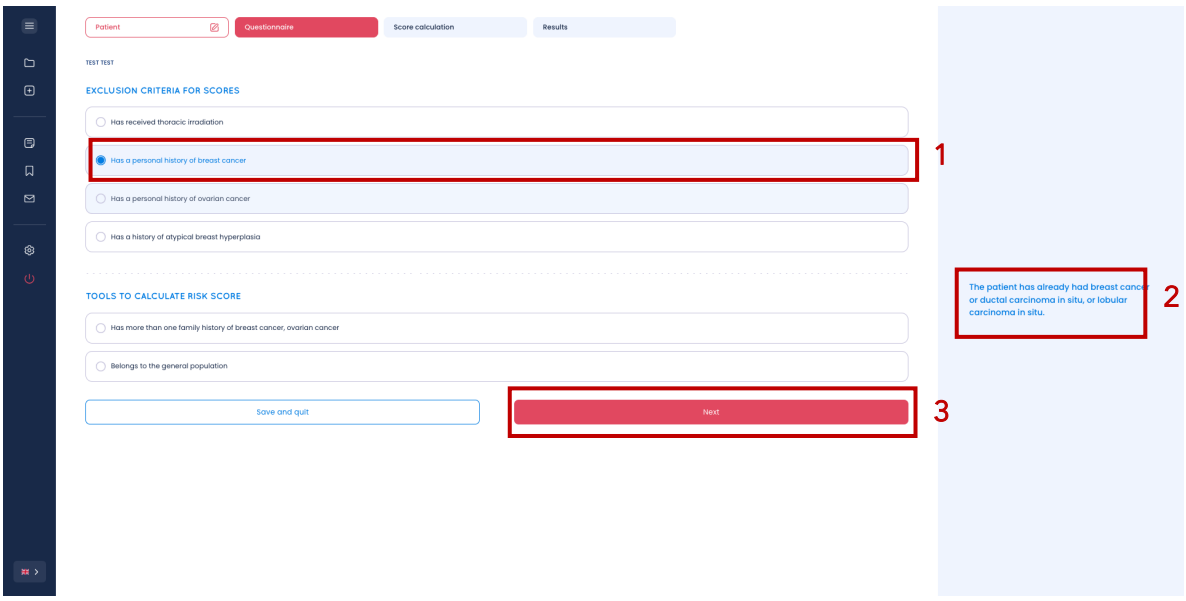
v2.8 For more information, visit www.mammorisk.com

3. Personal history of breast cancer

   a. Presentation

      If the patient has already had breast cancer or ductal carcinoma in situ, or lobular carcinoma in situ, the user will check the box “Has a personal history of breast cancer” (1). An explanatory sentence will then appear to ensure that the patient meets this criterion (2).

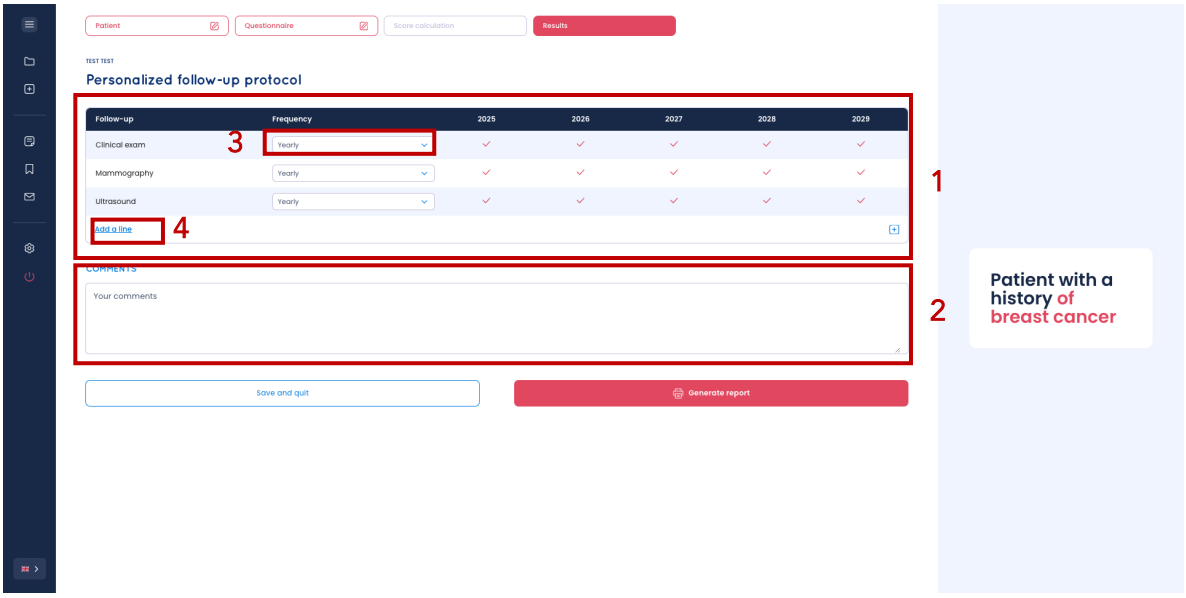
      If this is the case, they can click on the “Next” button (3).



b. Recommendations

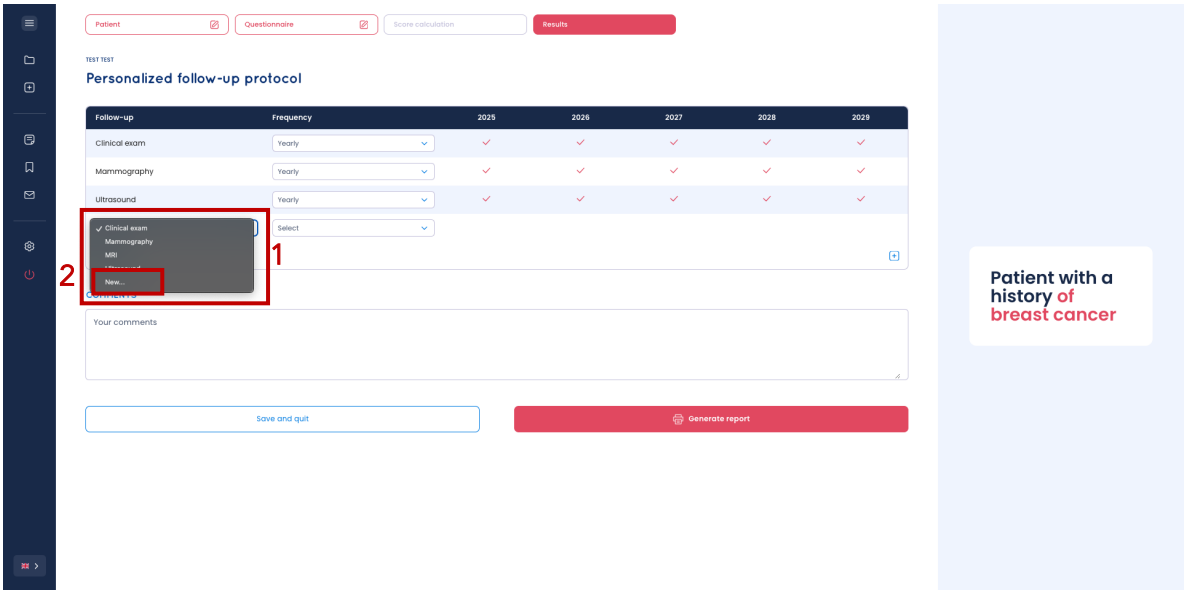
The user will access the recommendations in order to define the personalized patient monitoring protocol. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a "Comments" field to add other recommendations or remarks on the patient's profile.

They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account. The user can modify the frequency of examinations (3) and add more by clicking on "Add a line" (4).

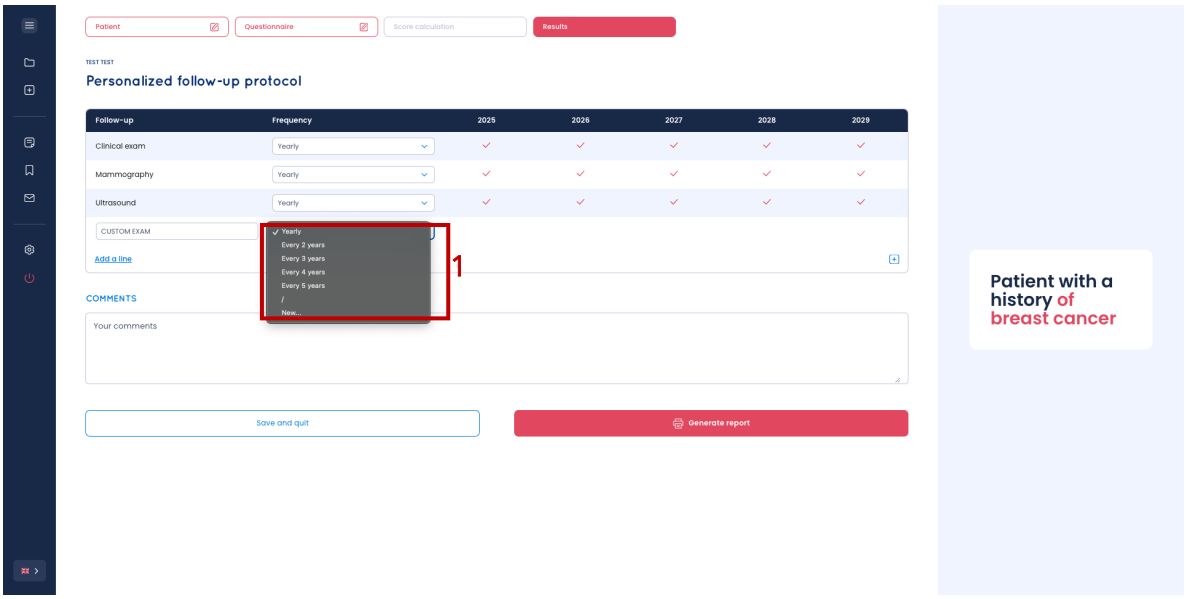


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If they wish to add an exam that is not present in the list, they can select “New” (2) and manually enter the name of the exam.



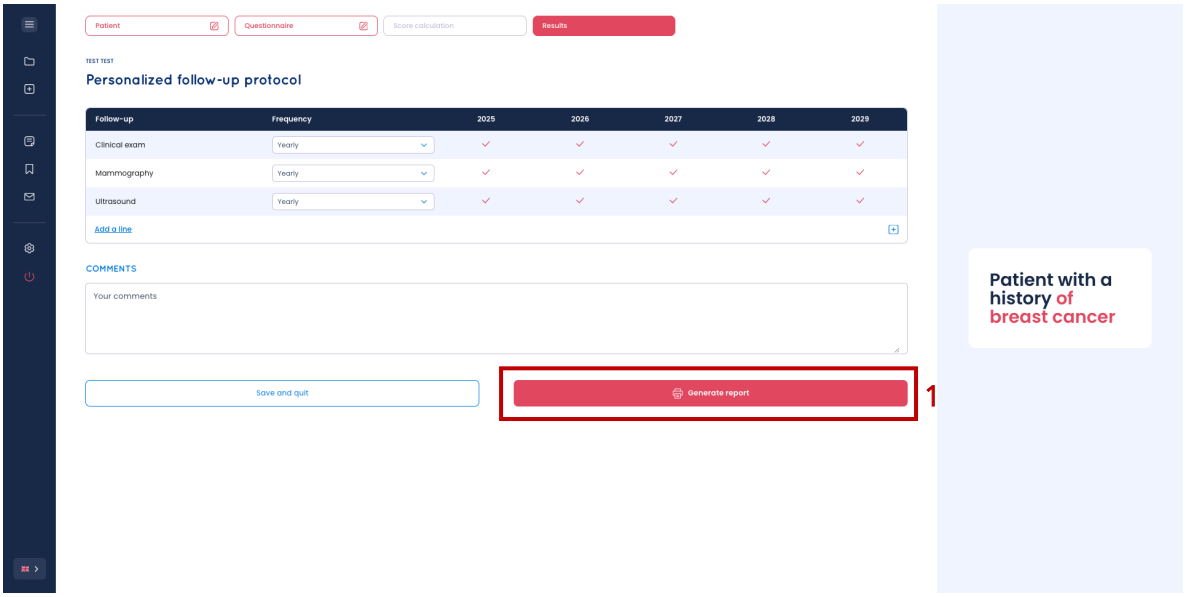
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.

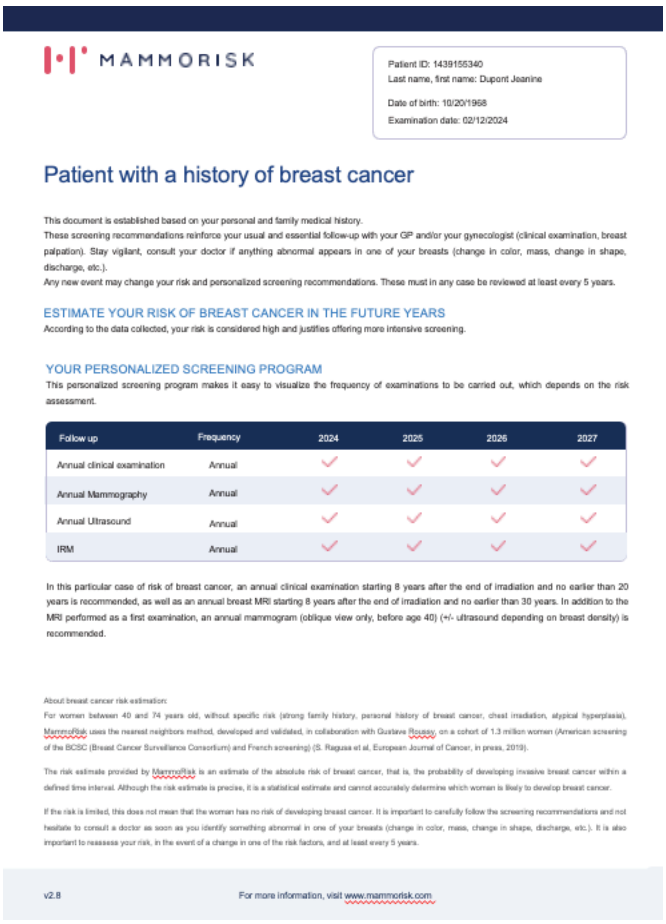


c. Generating a report

Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the “Generate report” button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional’s comments.





MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine
Date of birth: 10/20/1968
Examination date: 02/12/2024

Patient with a history of breast cancer

This document is established based on your personal and family medical history.
These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in any case be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS
According to the data collected, your risk is considered high and justifies offering more intensive screening.

YOUR PERSONALIZED SCREENING PROGRAM
This personalized screening program makes it easy to visualize the frequency of examinations to be carried out, which depends on the risk assessment.

Follow up	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓
IRM	Annual	✓	✓	✓	✓

In this particular case of risk of breast cancer, an annual clinical examination starting 8 years after the end of irradiation and no earlier than 20 years is recommended, as well as an annual breast MRI starting 8 years after the end of irradiation and no earlier than 30 years. In addition to the MRI performed as a first examination, an annual mammogram (oblique view only, before age 40) (+/- ultrasound depending on breast density) is recommended.

About breast cancer risk estimation:
For women between 40 and 74 years old, without specific risk (strong family history, personal history of breast cancer, chest irradiation, atypical hyperplasia), MammoRisk uses the nearest neighbors method, developed and validated, in collaboration with Gustave Roussy, on a cohort of 1.3 million women (American screening of the BCSC (Breast Cancer Surveillance Consortium) and French screening) (S. Ragusa et al, European Journal of Cancer, in press, 2019).

The risk estimate provided by MammoRisk is an estimate of the absolute risk of breast cancer, that is, the probability of developing invasive breast cancer within a defined time interval. Although the risk estimate is precise, it is a statistical estimate and cannot accurately determine which woman is likely to develop breast cancer.

If the risk is limited, this does not mean that the woman has no risk of developing breast cancer. It is important to carefully follow the screening recommendations and not hesitate to consult a doctor as soon as you identify something abnormal in one of your breasts (change in color, mass, change in shape, discharge, etc.). It is also important to reassess your risk, in the event of a change in one of the risk factors, and at least every 5 years.

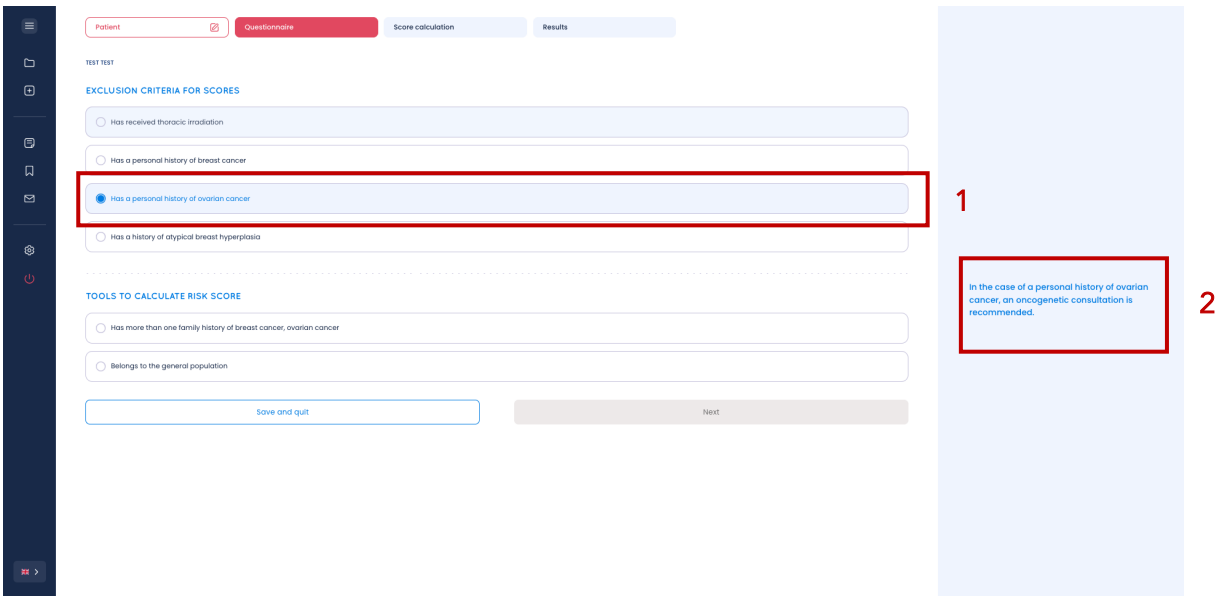
v2.8 For more information, visit www.mammorisk.com

4. Personal history of ovarian cancer

a. Presentation

If the patient has a personal history of ovarian cancer, the user will check the box “Has a personal history of ovarian cancer” (1).

The healthcare professional will not be able to click “Next” or generate a report. An explanatory sentence will then appear to inform the user that it is recommended to carry out a genetic counseling for this patient (2).

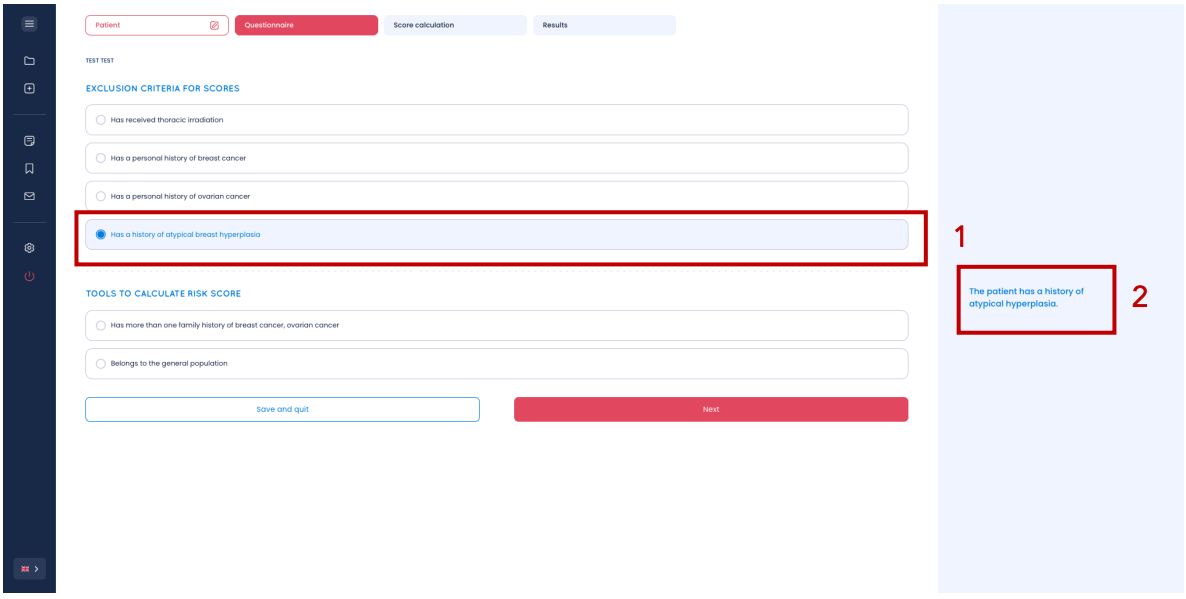


5. Previous case of atypical breast hyperplasia

a. Presentation

If the patient has a history of atypical hyperplasia, the user will check the box "Has a history of atypical hyperplasia of the breast" (1). An explanatory sentence will then appear to ensure that the patient meets this criterion (2).

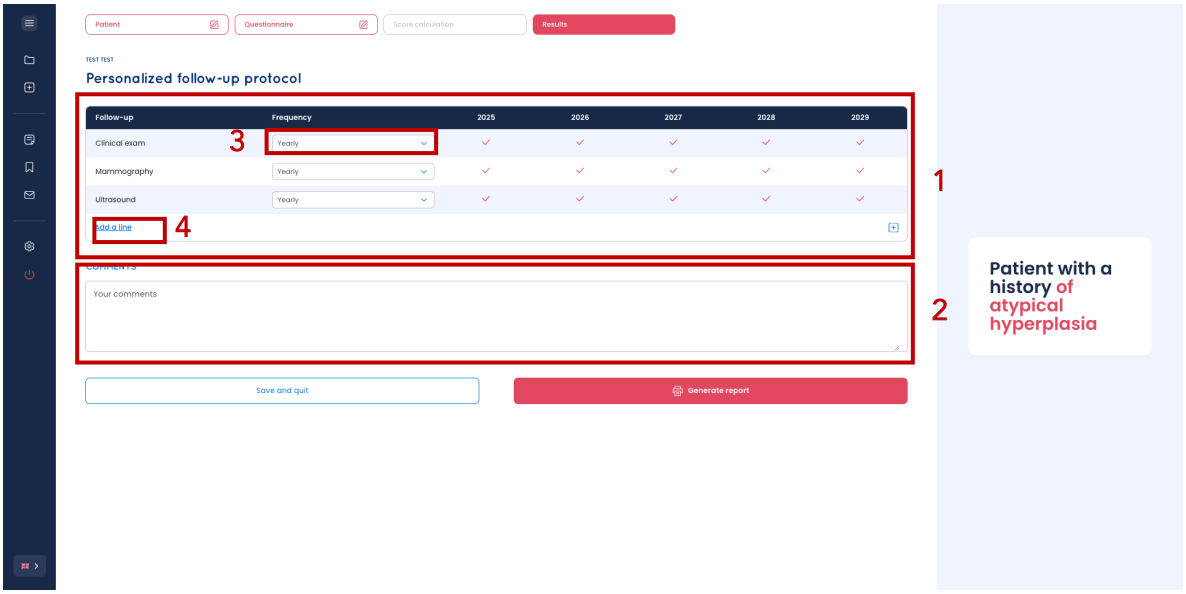
If this is the case, the user can click on the "Next" button (3).



b. Recommendations

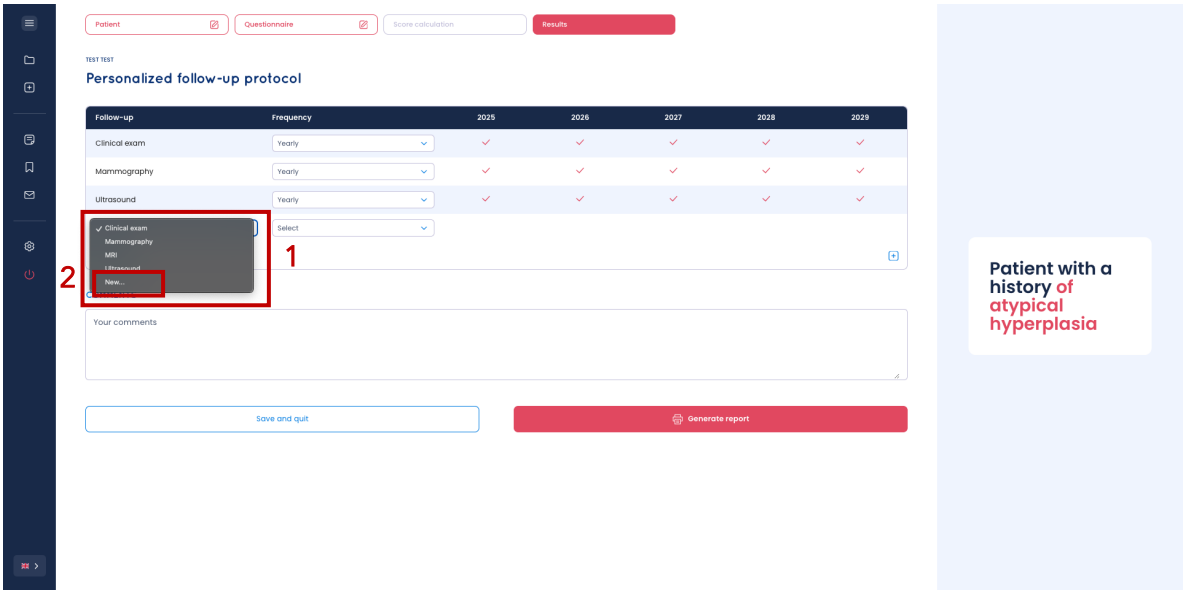
The user will access the recommendations in order to define the personalized patient monitoring protocol. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a "Comments" field to add other recommendations or remarks on the patient's profile.

They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account. The user can modify the frequency of examinations (3) and add more by clicking on "Add a line" (4).

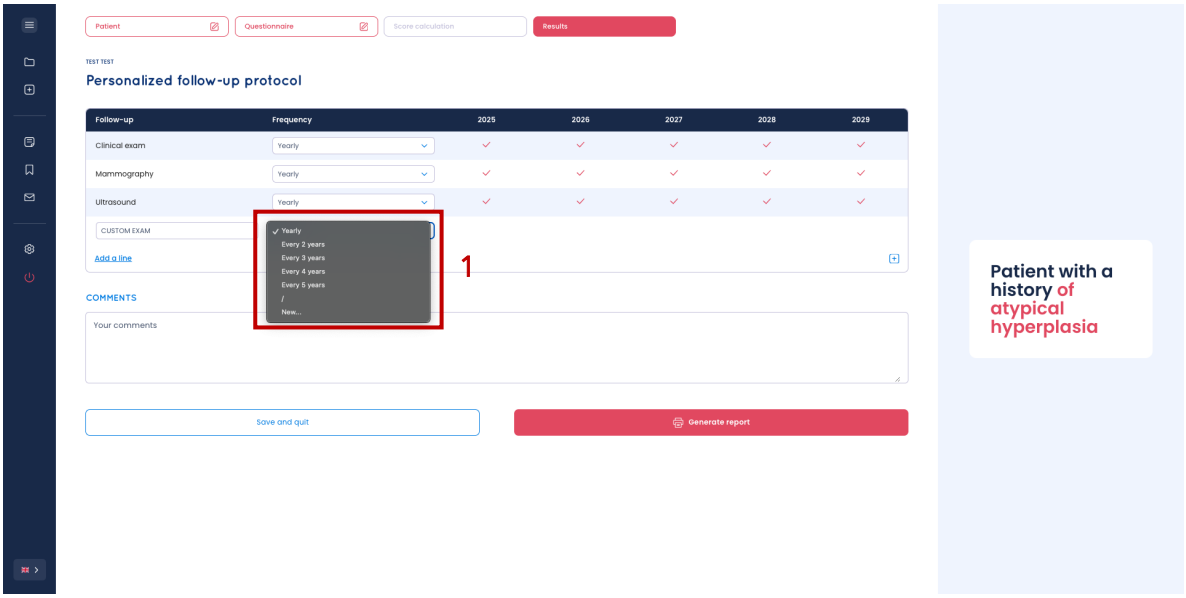


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If the user wishes to add an exam that is not present in the list, the user can select "New" (2) and manually enter the name of the exam.



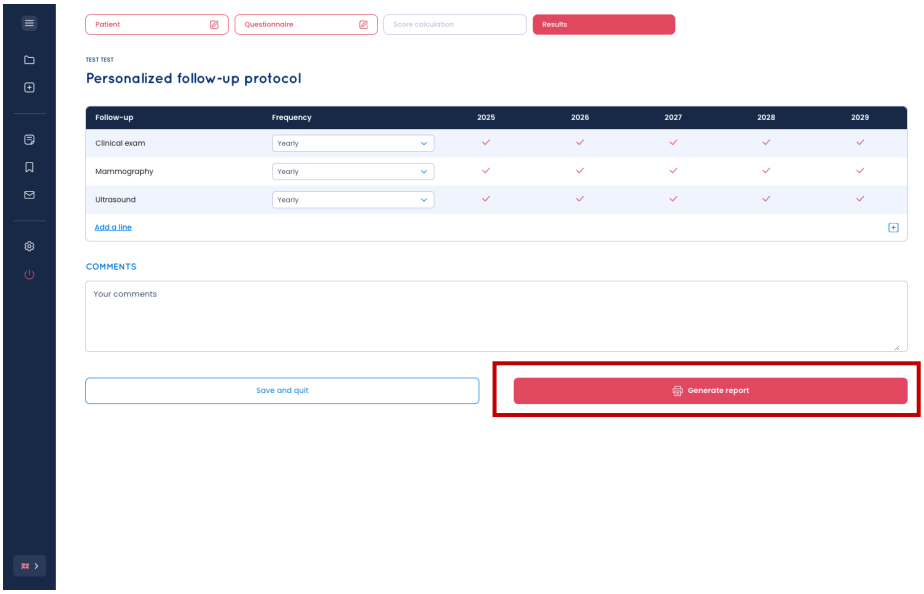
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.



c. Generating a report

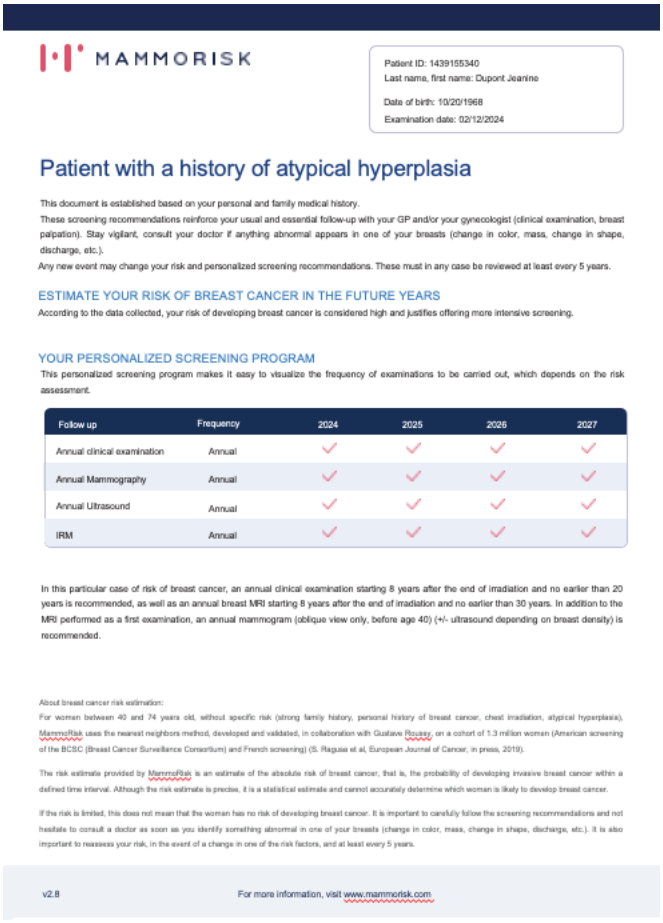
Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the "Generate report" button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional's comments.



1

Patient with a history of atypical hyperplasia



MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine
Date of birth: 10/20/1968
Examination date: 02/12/2024

Patient with a history of atypical hyperplasia

This document is established based on your personal and family medical history.
These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in any case be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS

According to the data collected, your risk of developing breast cancer is considered high and justifies offering more intensive screening.

YOUR PERSONALIZED SCREENING PROGRAM

This personalized screening program makes it easy to visualize the frequency of examinations to be carried out, which depends on the risk assessment.

Follow up	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓
IRM	Annual	✓	✓	✓	✓

In this particular case of risk of breast cancer, an annual clinical examination starting 8 years after the end of irradiation and no earlier than 20 years is recommended, as well as an annual breast MRI starting 8 years after the end of irradiation and no earlier than 30 years. In addition to the MRI performed as a first examination, an annual mammogram (oblique view only, before age 40) (+/- ultrasound depending on breast density) is recommended.

About breast cancer risk estimation:
For women between 40 and 74 years old, without specific risk (strong family history, personal history of breast cancer, chest irradiation, atypical hyperplasia), MammoRisk uses the nearest neighbors method, developed and validated, in collaboration with Gustave Roussy, on a cohort of 1.3 million women (American screening of the BCSC (Breast Cancer Surveillance Consortium) and French screening) (S. Ragusa et al, European Journal of Cancer, in press, 2019).

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If the risk is limited, this does not mean that the woman has no risk of developing breast cancer. It is important to carefully follow the screening recommendations and not hesitate to consult a doctor as soon as you identify something abnormal in one of your breasts (change in color, mass, change in shape, discharge, etc.). It is also important to reassess your risk, in the event of a change in one of the risk factors, and at least every 5 years.

v2.8

For more information, visit www.mammorisk.com

VII. General population score

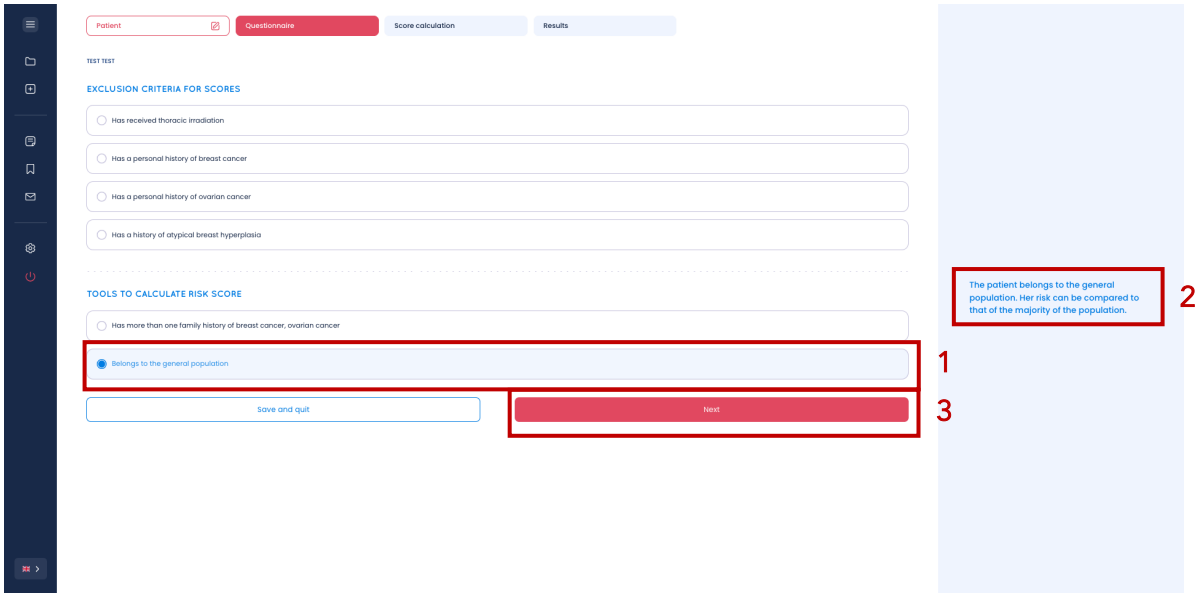
1. Presentation

The general population score allows the user to estimate the risk of developing breast cancer in a woman belonging to the general population, based on known risk factors.

Risk score calculation: The general population score, developed by Predilife, uses a non-parametric deterministic method. This algorithm gathers similar profiles using distance calculations within a database. The database used is a subset of the BCSC (Breast Cancer Surveillance Consortium) cohort, the largest prospective cohort worldwide dedicated to breast cancer. This subset includes 629,229 American women aged 40 to 74 from the general population, for whom data on age, biopsy history, first-degree family history, and breast density were available. These women were followed over a five-year period, during which breast cancer diagnoses were systematically recorded. The method compares a given woman's risk factor profile with those of other women within a cohort, looking for the most similar profiles and monitoring the outcomes of these women over a period of time.

If the patient does not meet exclusion criteria and has not a significant family history (more than one first-degree relative with breast cancer history), the user will check the box "Belongs to the general population" (1). An explanatory sentence will then appear to verify that the patient corresponds to this scenario (2).

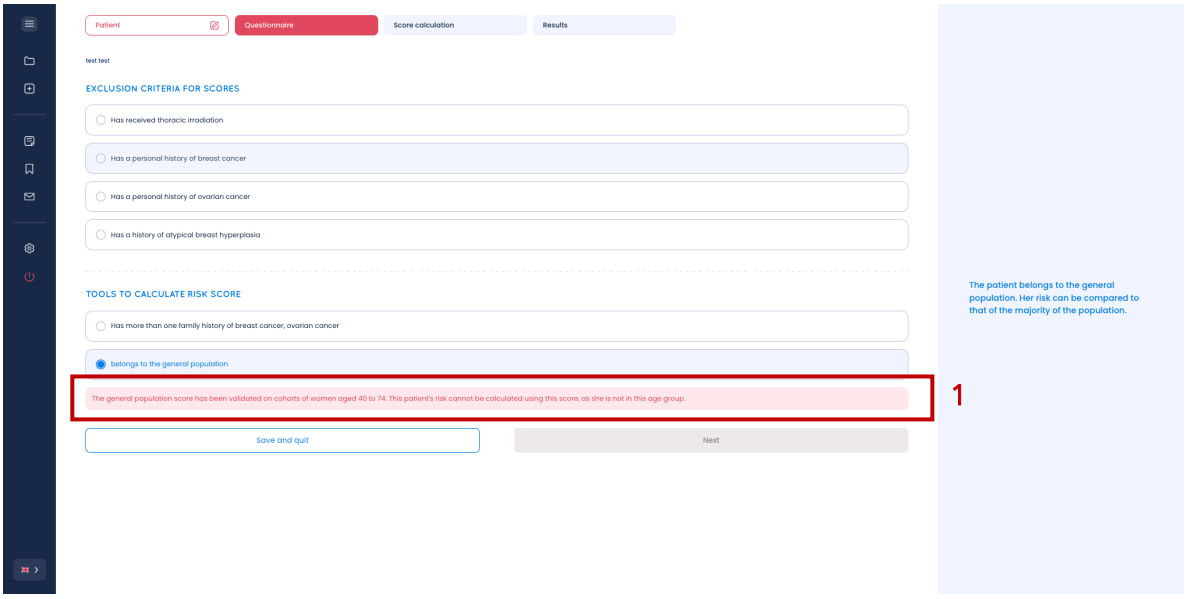
If this is the case, the user can click on the "Next" button (3)



If the patient is not of the required age (age 40 to 74 years inclusive) when her breast cancer risk is assessed, an error message will be displayed with the following text (1):

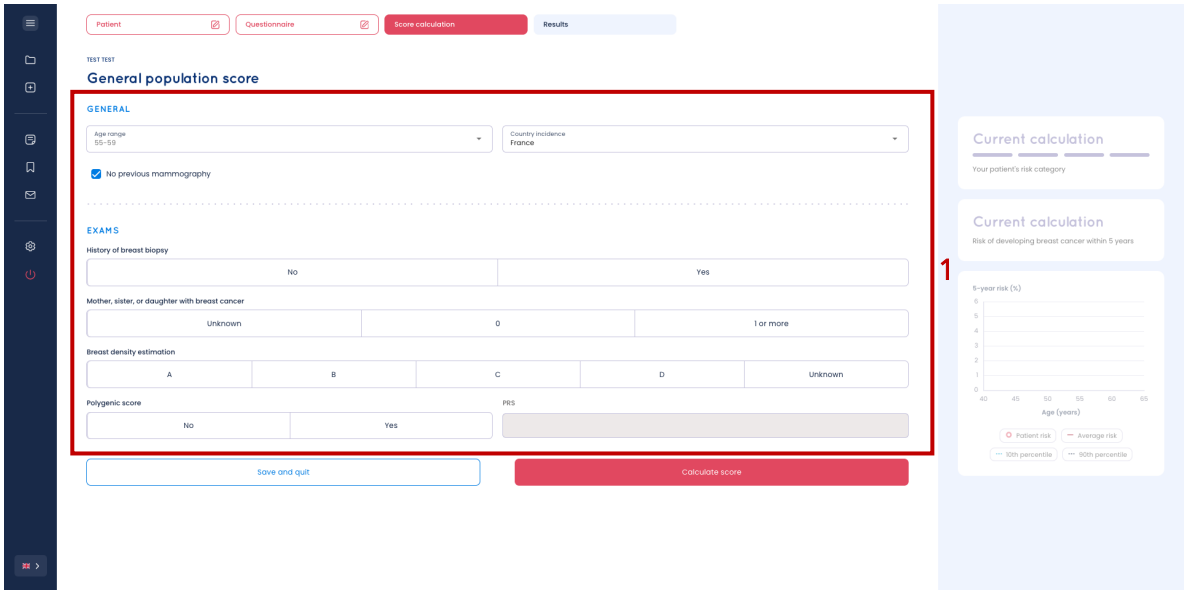
“The general population score was validated on cohorts of women aged 40 to 74. This patient's risk cannot be calculated using this score because she is not in this age group. »

The user will not be able to use this score, because the “Next” button will be blocked.



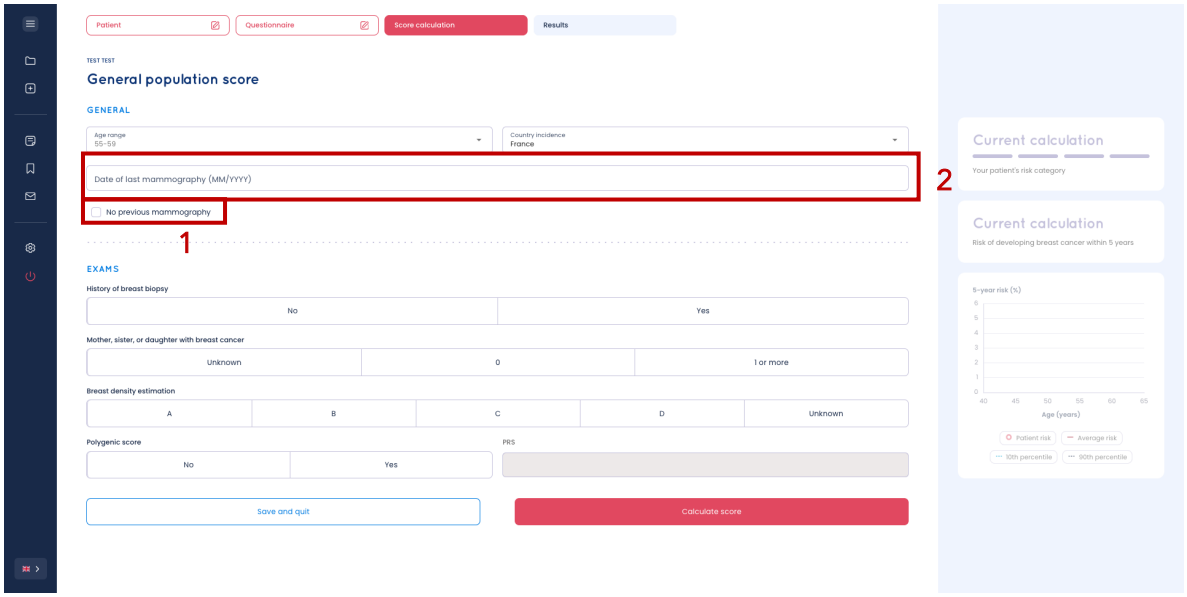
2. Questionnaire

The user must complete all fields of the questionnaire in order to be able to assess the risk of breast cancer using the general population score (1).

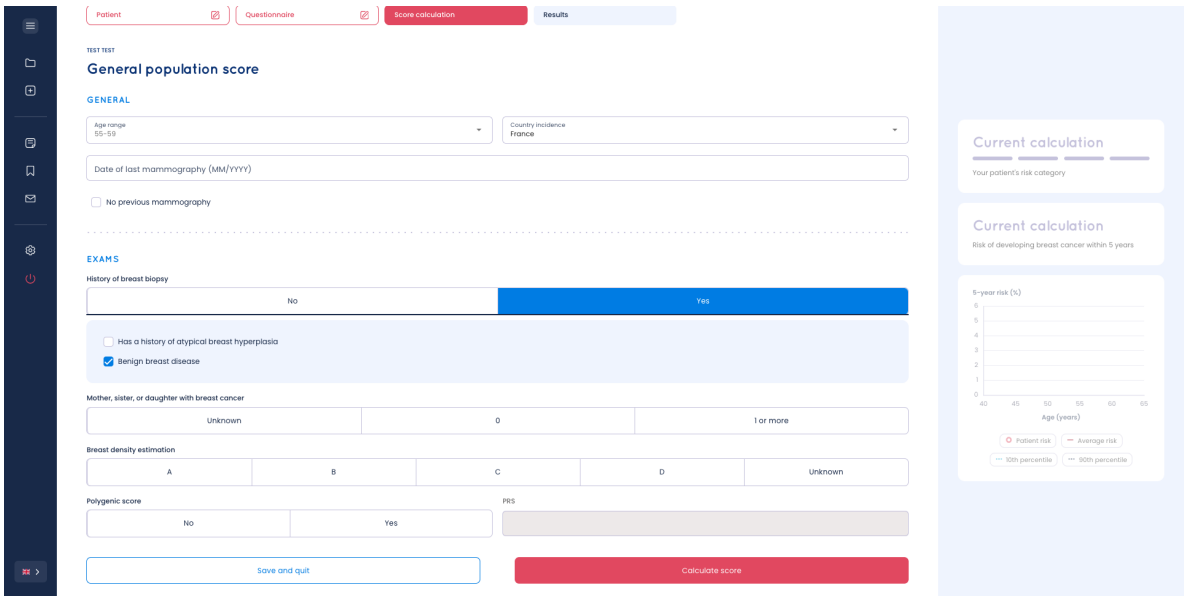


If the patient has already had a mammogram, the user can uncheck box (1). The user can then enter the date of this examination by indicating the month and year (2).

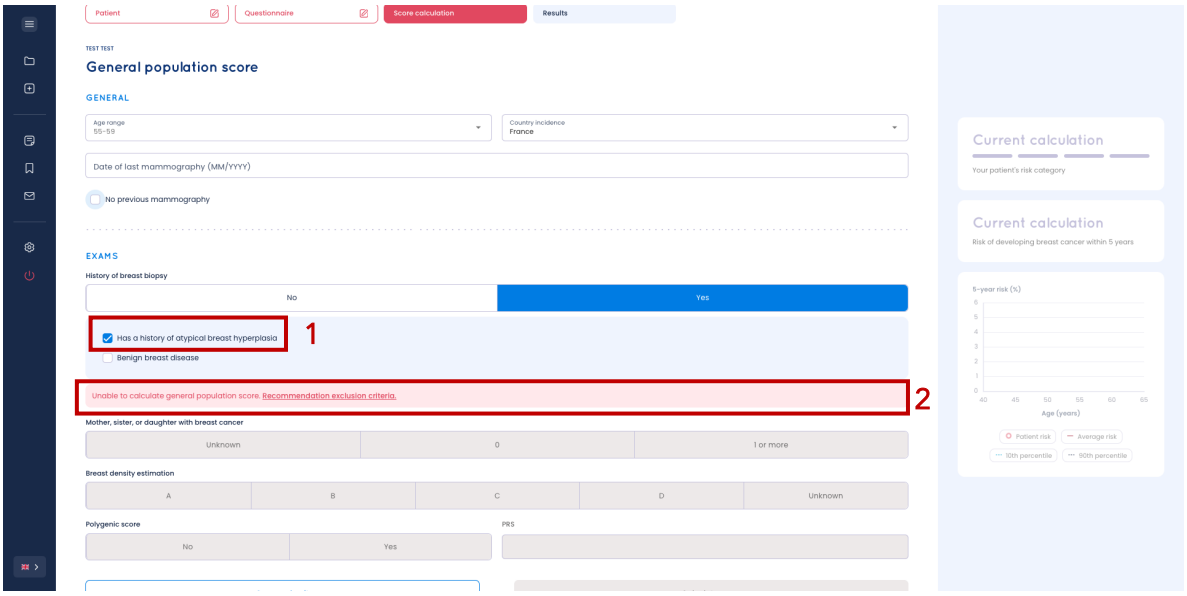
This makes it possible to adapt the follow-up recommendations by adjusting the date of completion of the examination according to the frequency defined by the user.



If the patient has had a biopsy, a sub-question is displayed to check whether it is benign breast disease.



If this is not the case, the user must check the box “History of atypical breast hyperplasia” (1). It will then not be able to calculate the general population risk score and will be directed towards the exclusion criterion “History of atypical breast hyperplasia”, with the associated recommendations (2).

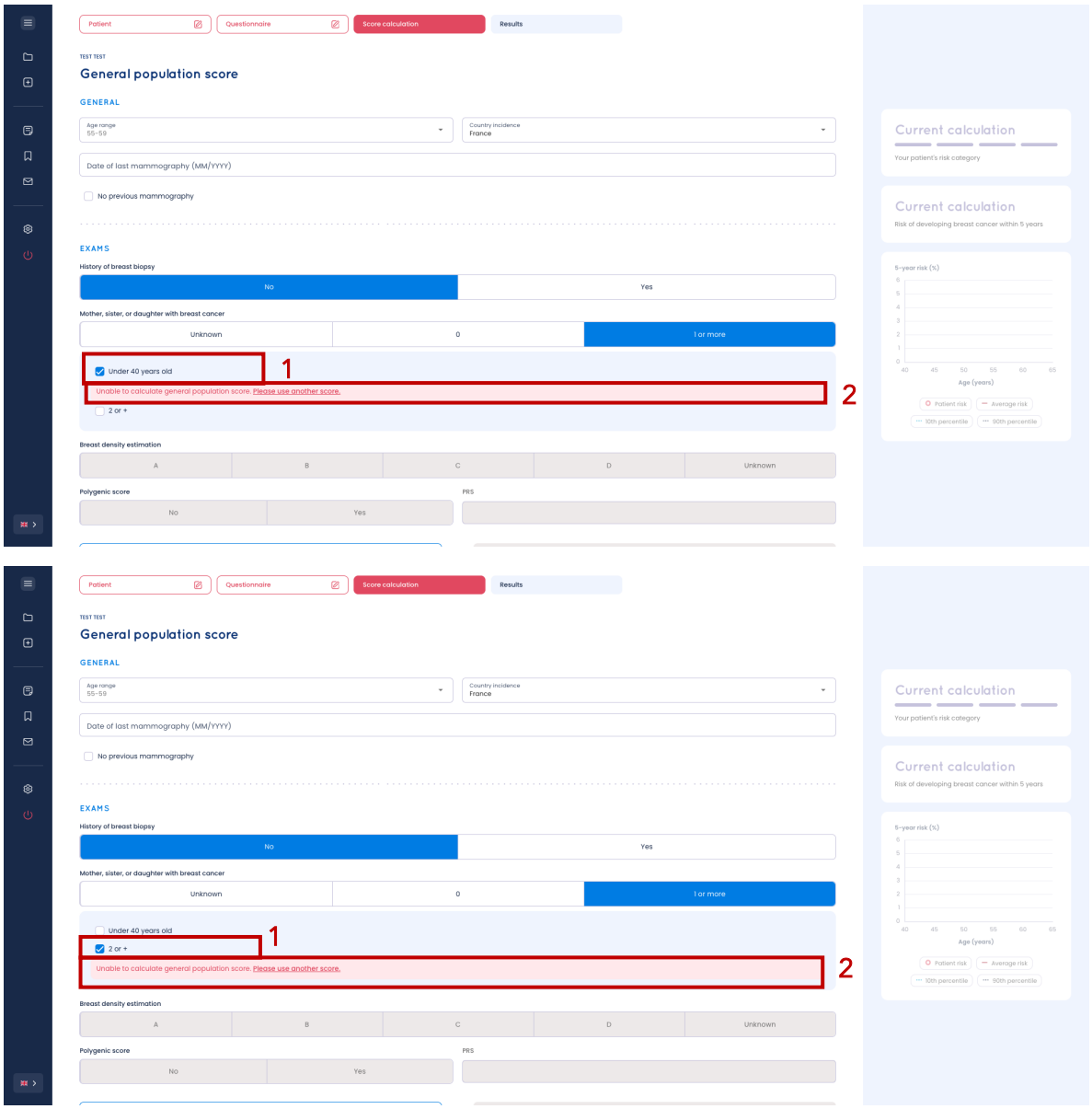


If the patient has two or more first-degree relatives (mother, sister, daughter) with breast cancer history, a sub-question will be displayed to check:

- If none of the family breast cancer cases occurred before age 40,
- Or if there are not two or more first degree antecedents.

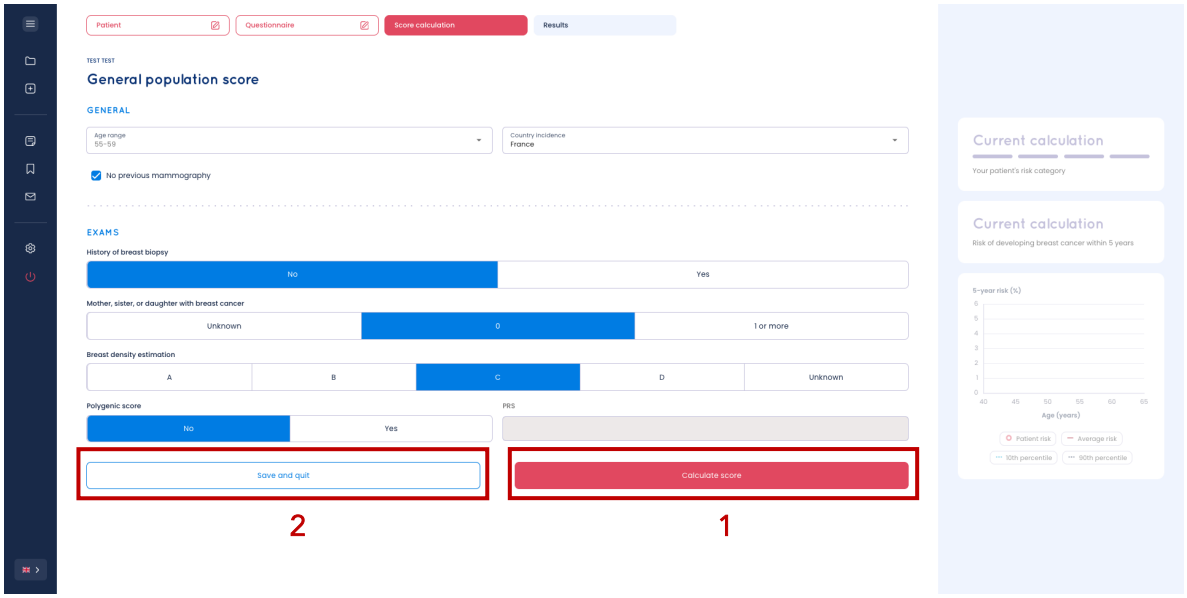
If one of these cases turns out to be true, the user must check the box corresponding to the patient's profile, i.e. "Age less than 40 years" or "2 or more" (1).

It will then not be able to calculate the general population risk score and will be directed towards other available risk scores: the Tyrer-Cuzick score and the Eisinger score (for a healthcare professional working in France) (2).



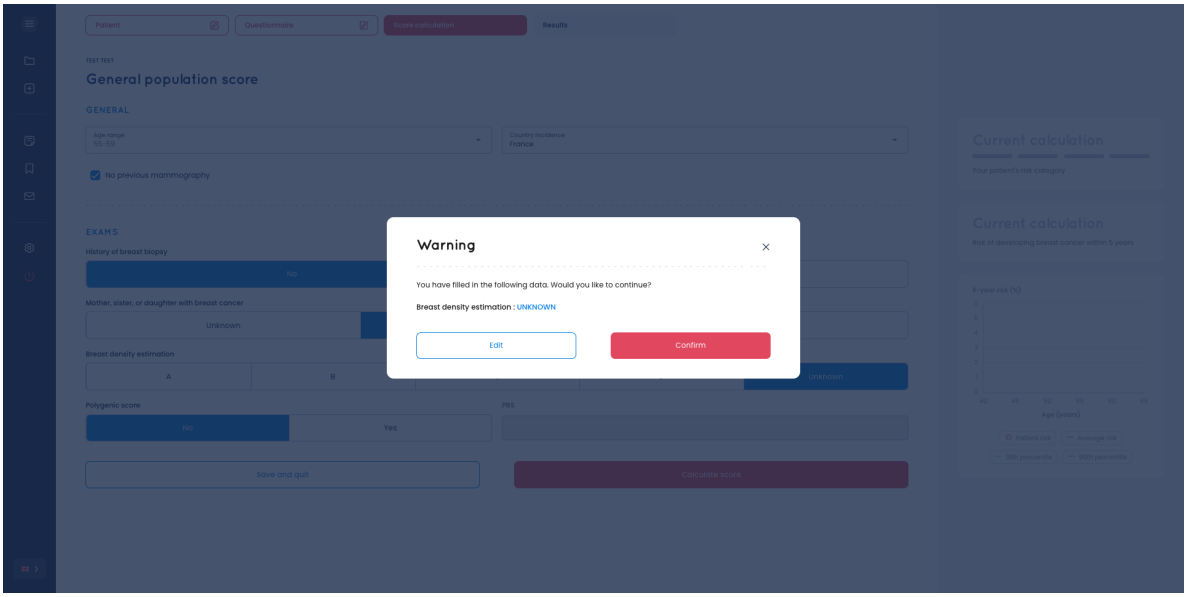
When the user has fully completed the questionnaire, they can click on “Calculate score” (1) to assess the woman’s 5-year risk. If information data such as breast density or PRS score is missing, the healthcare professional can click “Save and quit” (2) to save the exam and the information entered until this data becomes available.

Once the results are known, they can reselect the patient's file as well as the examination, which will have the status "In progress", in order to resume the risk assessment.



If the user has indicated “Unknown” in a field of the questionnaire, a pop-up will be displayed to warn them when they attempt to calculate the risk score.

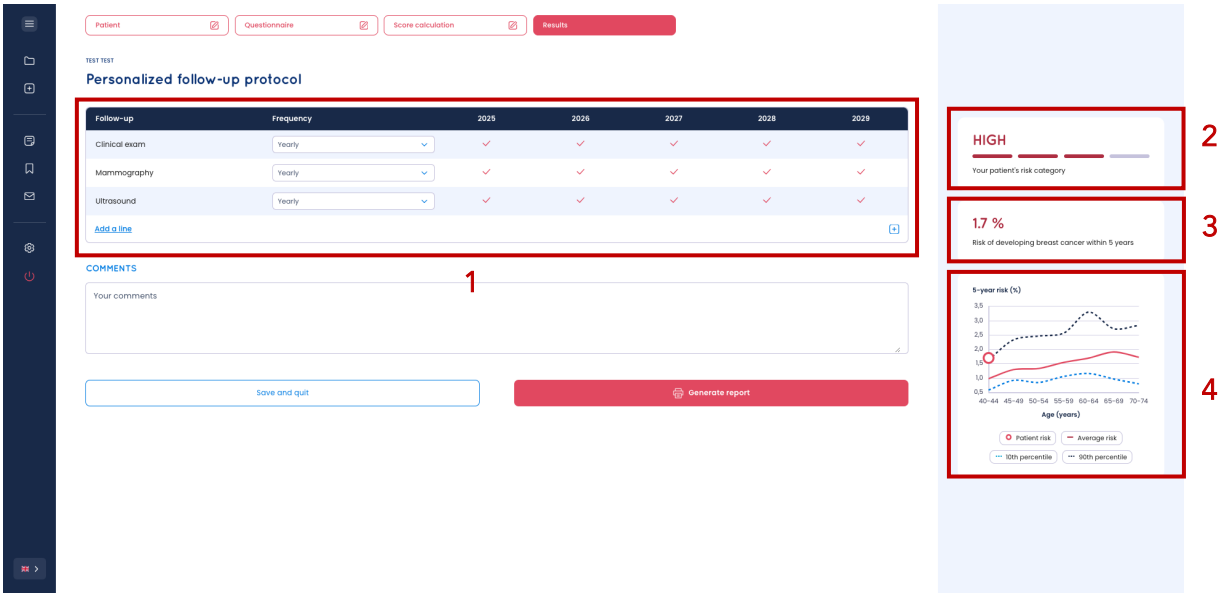
- If they click on “Edit”, they will be redirected to the questionnaire in order to update it.
- If they click on “Confirm”, the risk score will be calculated from the information provided by the user.



3. Risk calculation and visualization of results

When the user clicks on "Calculate score" for the patient, they will be redirected to the "Results" page displaying:

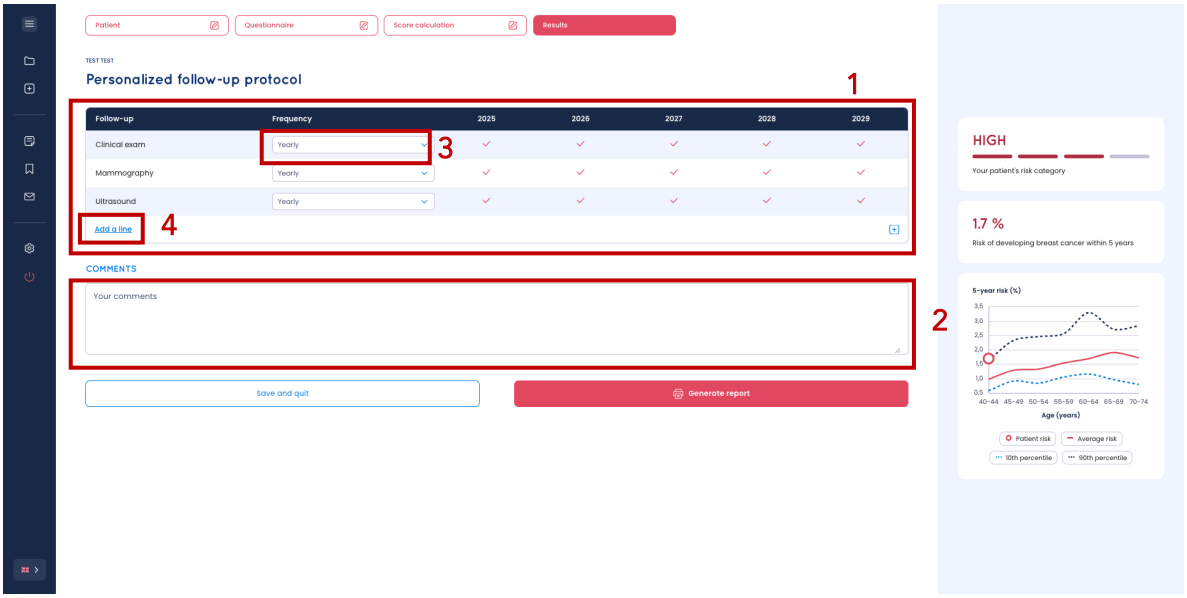
- The recommendations associated with the calculated risk score and defined by default by the healthcare professional when the account is created (1).
- The patient's risk category (moderate risk, intermediate risk, high risk, very high risk) (2).
- The patient's 5-year risk score (3).
- A graph allows the patient to be located (pink circle) in relation to the general population (pink curve) and to the 10th and 90th percentiles (dotted curves) (4).



4. Recommendations

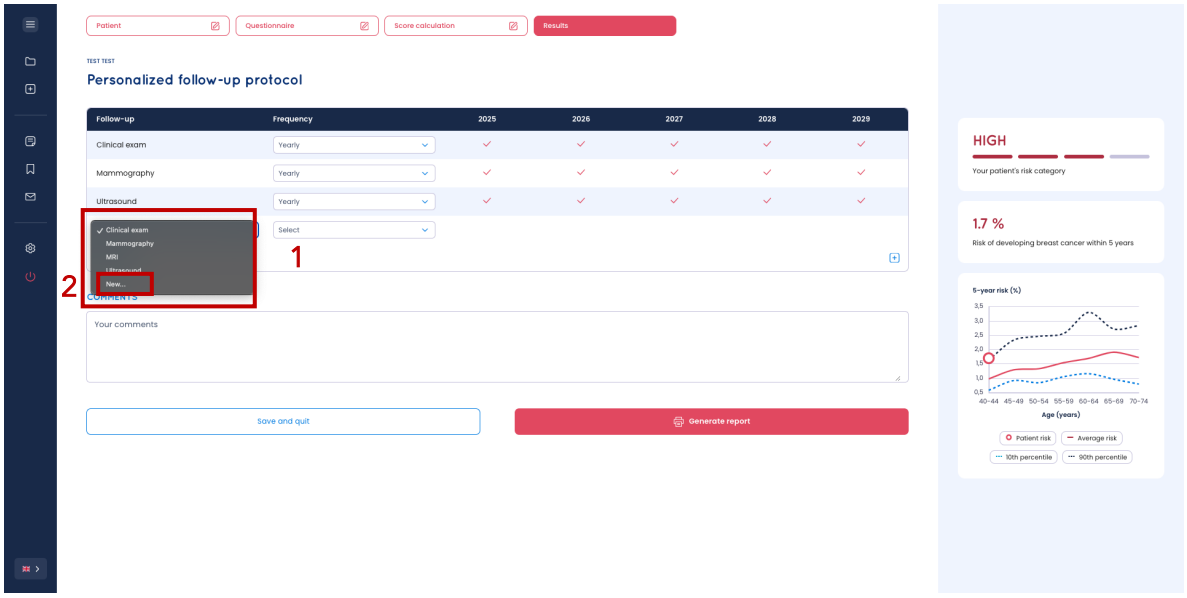
The user will access the recommendations in order to define the personalized patient monitoring protocol. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a "Comments" field to add other recommendations or remarks on the patient's profile.

They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account. The user can modify the frequency of examinations (3) and add more by clicking on "Add a line" (4).

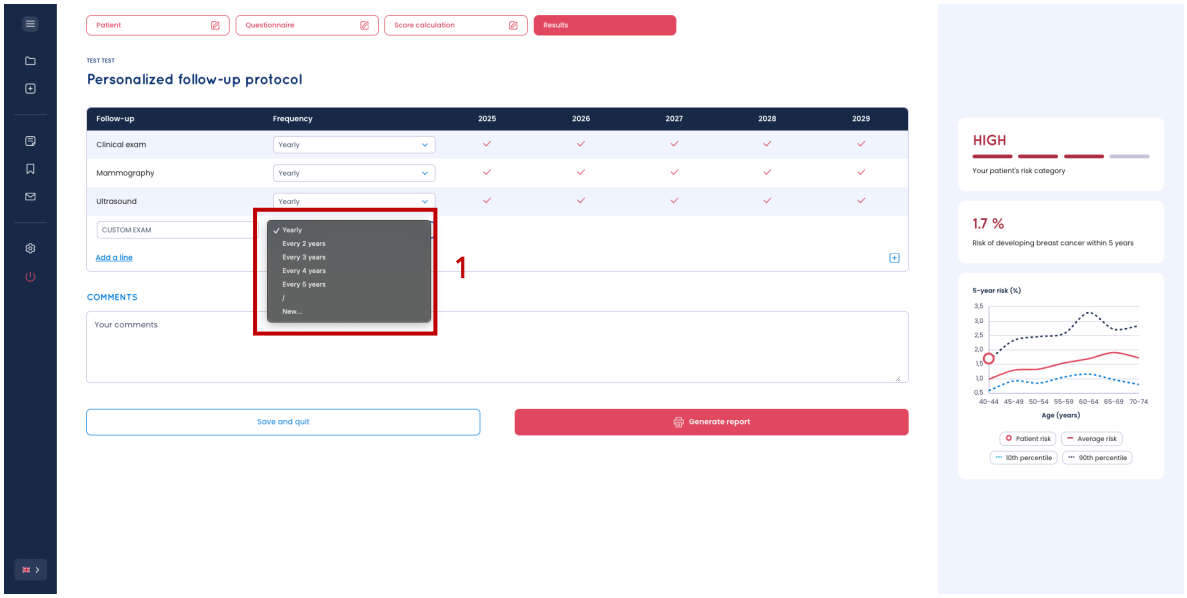


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If they wish to add an exam that is not present in the list, they can select “New” (2) and manually enter the name of the exam.



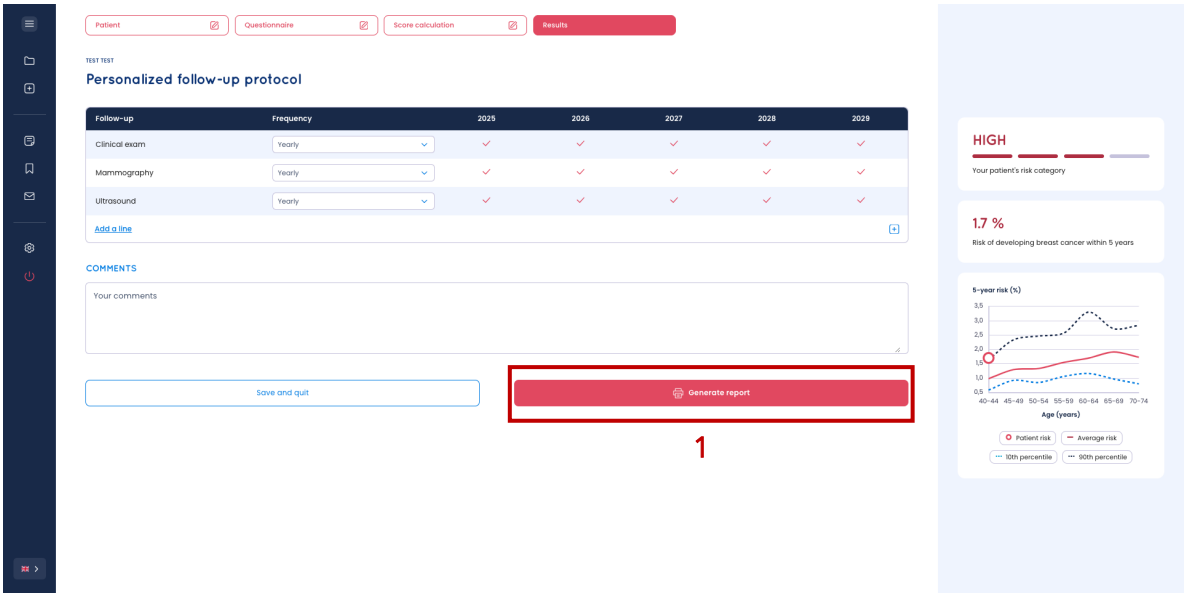
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.

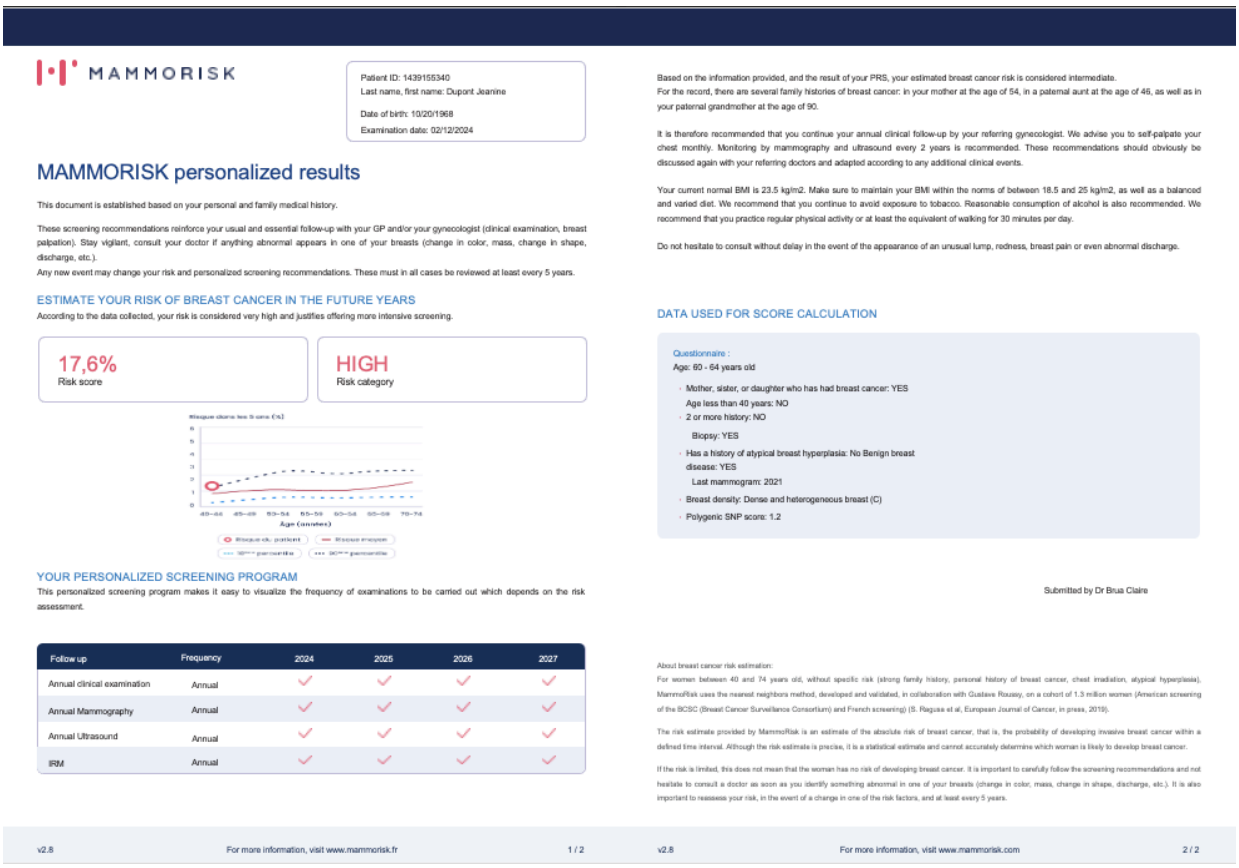


5. Generating a report

Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the “Generate report” button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional's comments.




MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine
Date of birth: 10/20/1968
Examination date: 02/12/2024

MAMMORISK personalized results

This document is established based on your personal and family medical history.

These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in all cases be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS

According to the data collected, your risk is considered very high and justifies offering more intensive screening.

17,6%
Risk score

HIGH
Risk category

YOUR PERSONALIZED SCREENING PROGRAM

This personalized screening program makes it easy to visualize the frequency of examinations to be carried out which depends on the risk assessment.

Follow up	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓
IRM	Annual	✓	✓	✓	✓

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Based on the information provided, and the result of your PRS, your estimated breast cancer risk is considered intermediate.
For the record, there are several family histories of breast cancer: in your mother at the age of 54, in a paternal aunt at the age of 46, as well as in your paternal grandmother at the age of 90.

It is therefore recommended that you continue your annual clinical follow-up by your referring gynecologist. We advise you to self-palpate your chest monthly. Monitoring by mammography and ultrasound every 2 years is recommended. These recommendations should obviously be discussed again with your referring doctors and adapted according to any additional clinical events.

Your current normal BMI is 23,5 kg/m2. Make sure to maintain your BMI within the norms of between 18.5 and 25 kg/m2, as well as a balanced and varied diet. We recommend that you continue to avoid exposure to tobacco. Reasonable consumption of alcohol is also recommended. We recommend that you practice regular physical activity or at least the equivalent of walking for 30 minutes per day.

Do not hesitate to consult without delay in the event of the appearance of an unusual lump, redness, breast pain or even abnormal discharge.

DATA USED FOR SCORE CALCULATION

Questionnaire :
Age: 60 - 64 years old
- Mother, sister, or daughter who has had breast cancer: YES
  Age less than 40 years: NO
- 2 or more history: NO
  Biopsy: YES
- Has a history of atypical breast hyperplasia: No Benign breast disease: YES
  Last mammogram: 2021
- Breast density: Dense and heterogeneous breast (C)
- Polygenic SNP score: 1.2

Submitted by Dr Brua Claire

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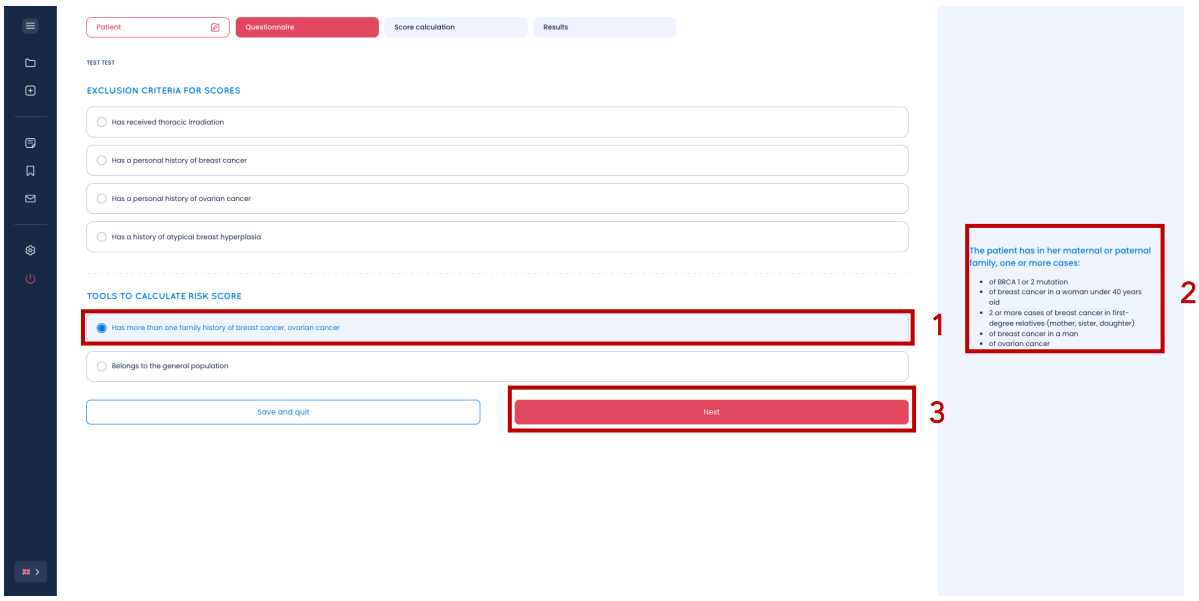
VIII. Significant family history-based risk score

1. Presentation

The scores intended for patients with a significant family history (more than one first-degree relative with breast cancer history) are used either to assess the risk of developing breast cancer with the Tyrer-Cuzick score, or to assess whether or not the patient should have a genetic counseling with the Eisinger score (the score is only available to healthcare professionals practicing in France).

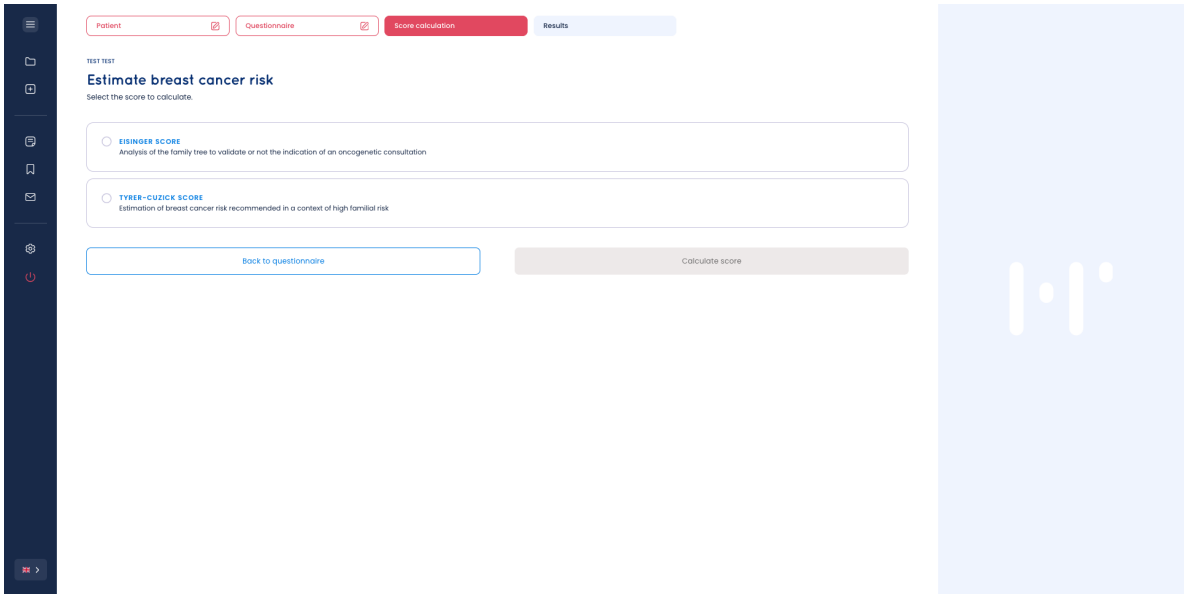
If the patient does not meet any exclusion criteria and has a significant family history, specifically more than one first-degree relative (mother, sister, daughter) with breast cancer history, the user will check the box “Has several family histories of breast cancer, ovarian cancer or breast cancer” (1). An explanatory sentence will then be displayed to confirm that the patient matches this scenario (2).

If so, the user can click on the “Next” button (3).



When the healthcare professional clicks on the "Next" button, two choices will be available to him depending on the configuration of his account:

- If the healthcare professional practices in France and has the Eisinger score accessible, they will have to choose between the Eisinger score and the Tyrer-Cuzick score.
- If the healthcare professional does not practice in France, they will be directly referred to the Tyrer-Cuzick score.



2. Tyrer-Cuzick score

a. Presentation

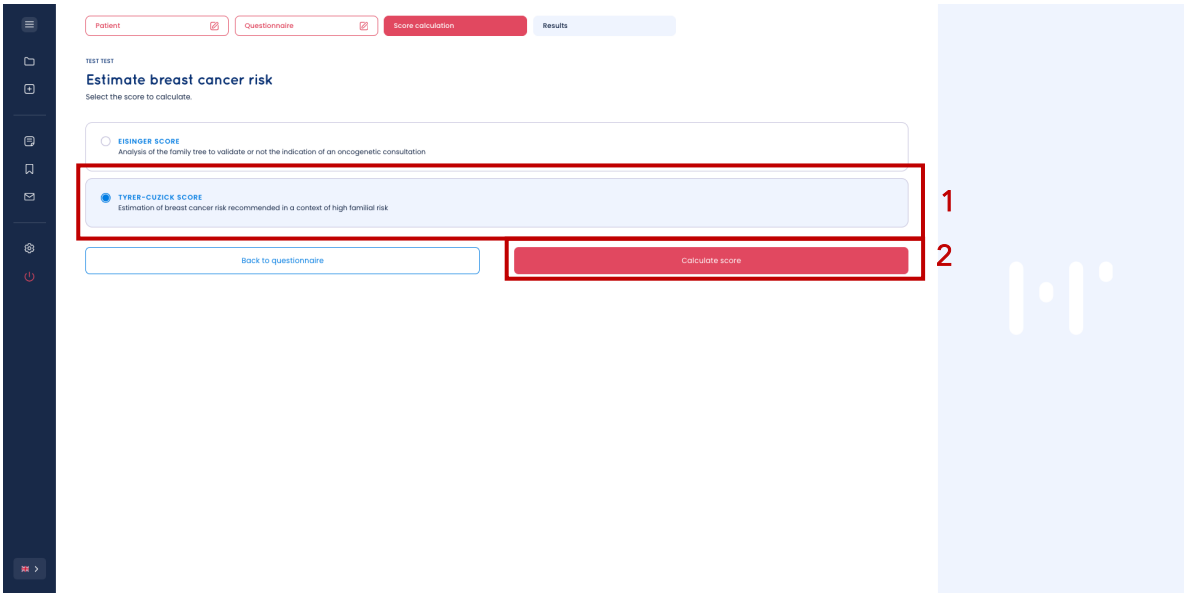
The Tyrer-Cuzick score allows the user to assess the risk of women who do not belong to the general population.

Risk score calculation: The Tyrer-Cuzick score is used to assess genetic risk (including BRCA mutation) via a Bayesian approach based on family history, and then incorporates this result with other factors (age, history, etc.) in a logistic regression to estimate the overall risk expressed as an absolute risk over a 5-year period.

For information regarding the performance of this risk score, please refer to the 'Claim regarding the performance' section.

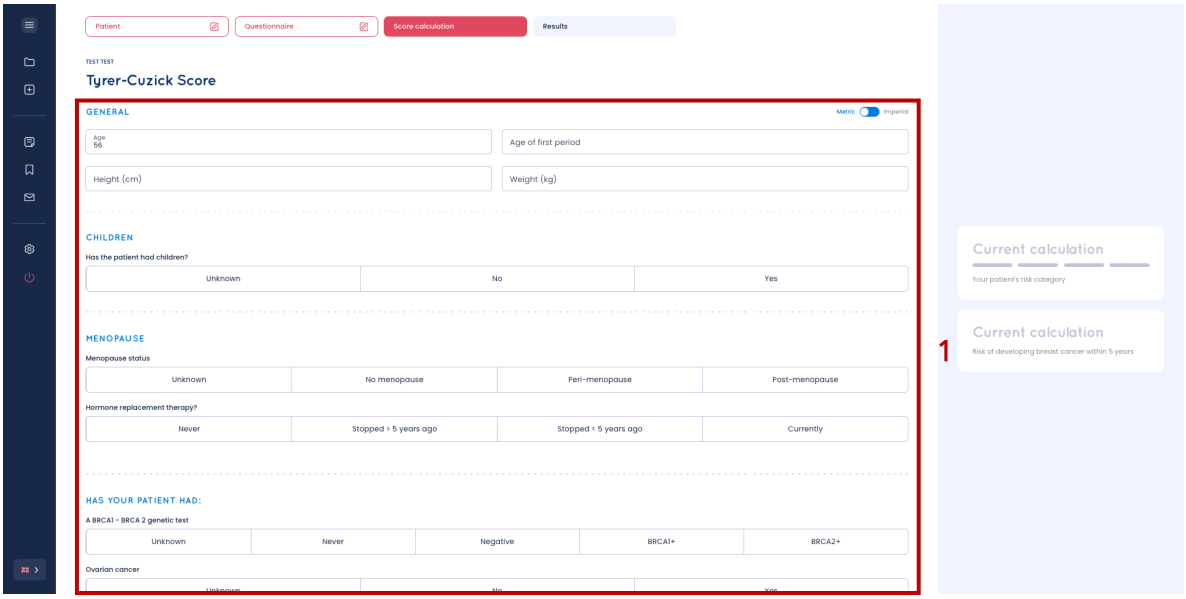
If the patient does not meet any exclusion criteria and has a significant family history, including more than one first-degree relative (mother, sister, daughter) with a history of breast cancer, the user should check the “Tyrer Cuzick” box (1).

If so, the user can click on the “Next” button (2).



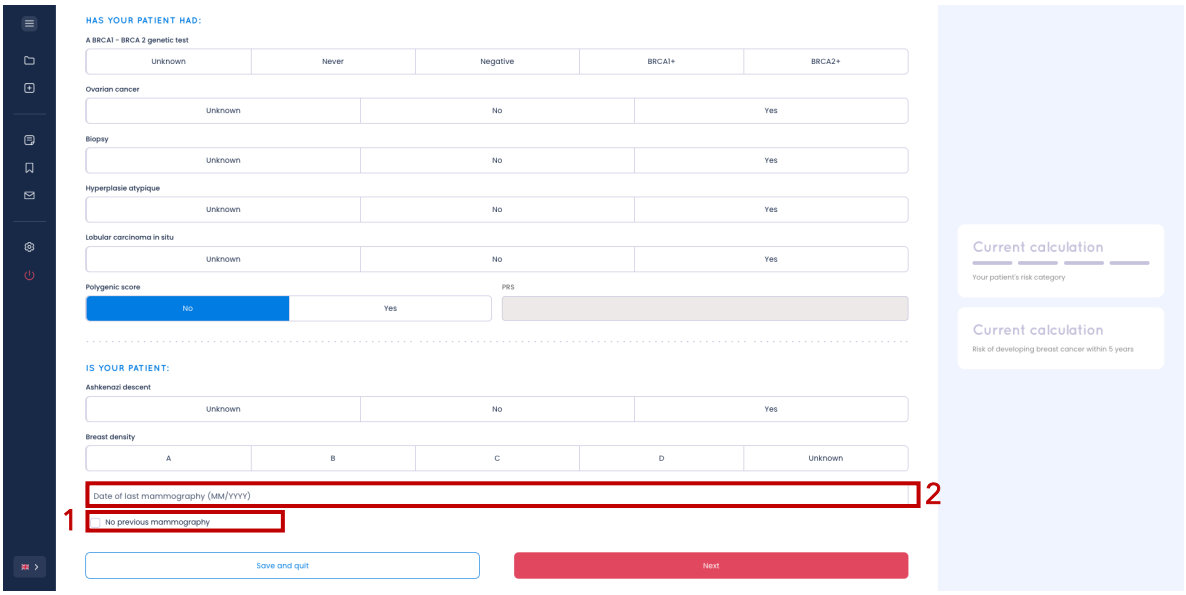
b. Questionnaire

The user must complete all fields of the questionnaire in order to be able to assess the risk of breast cancer using the Tyrer-Cuzick score (1).



If the patient has already had a mammogram, the user can uncheck box (1). They can then enter the date of this examination by indicating the month and year (2).

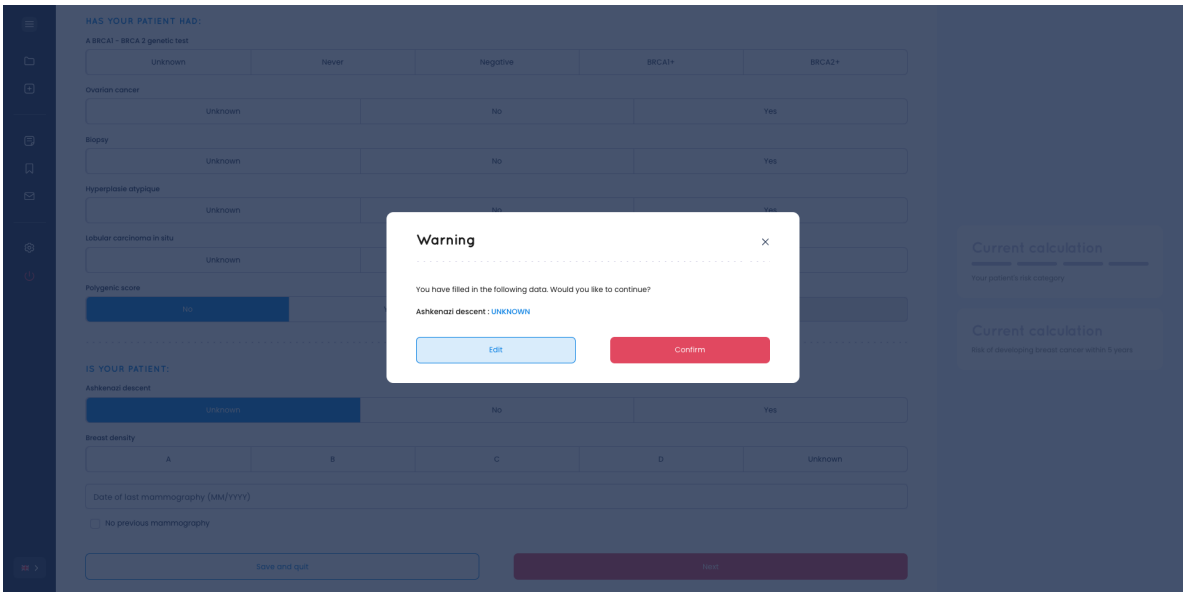
This makes it possible to adapt the follow-up recommendations by adjusting the date of completion of the examination according to the frequency defined by the user.



If the user has indicated “Unknown” in a field of the questionnaire, a pop-up will be displayed to warn them when they attempt to calculate the risk score.

- If they click on “Edit”, the user will be redirected to the questionnaire in order to update it.
- If they click on “Confirm”, the user will be redirected to the page to enter family members.

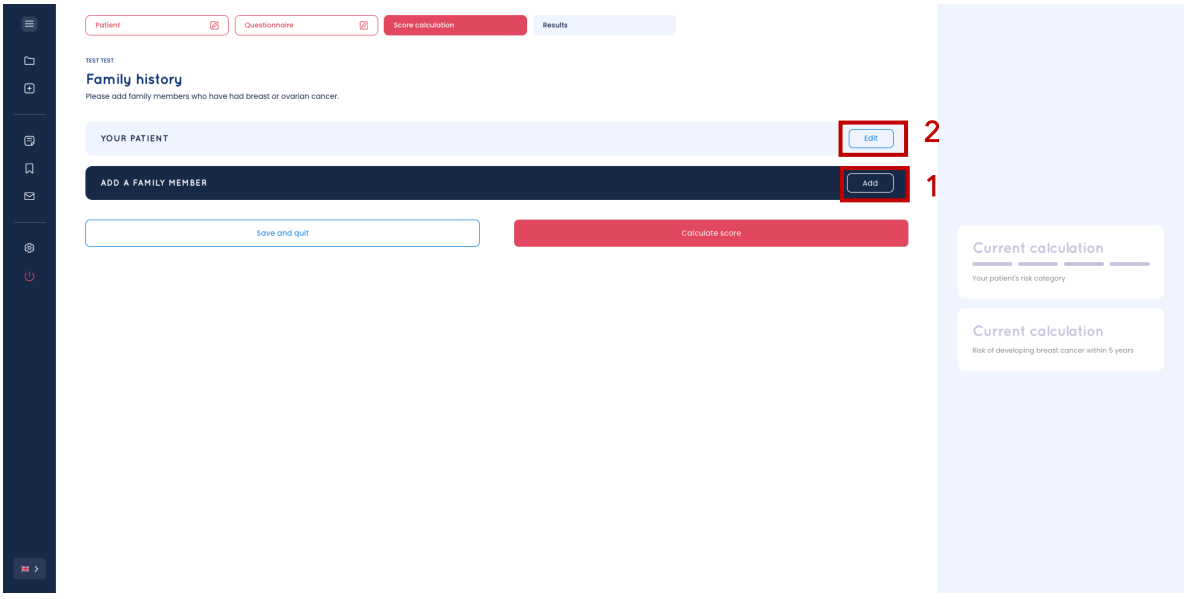
> ⚠ If there is no answer to a question (empty field), a median value will be automatically used to calculate the risk score.



c. Adding family member

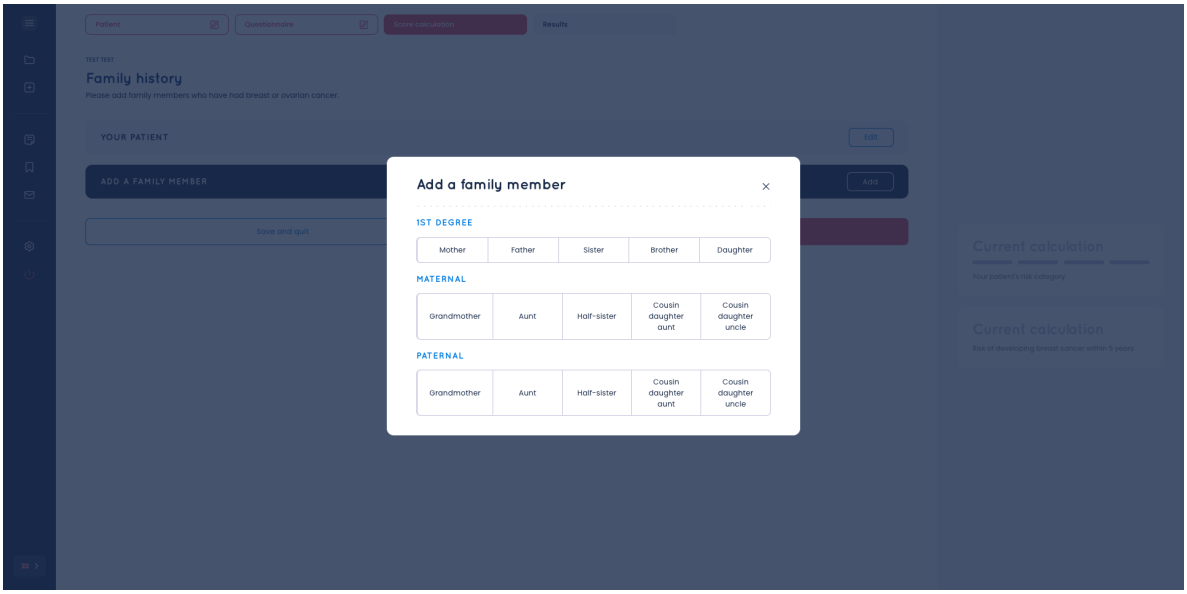
The user must enter the family members of the patient who has or has had breast or ovarian cancer, by clicking on the "Add" button (1).

If they wish to return to the questionnaire to modify or verify information entered, they must click on "Modify" (2). They will then be redirected to the questionnaire.



A pop-up is displayed to the user to allow them to select the family member(s) who have had breast or ovarian cancer. Members are divided into three categories:

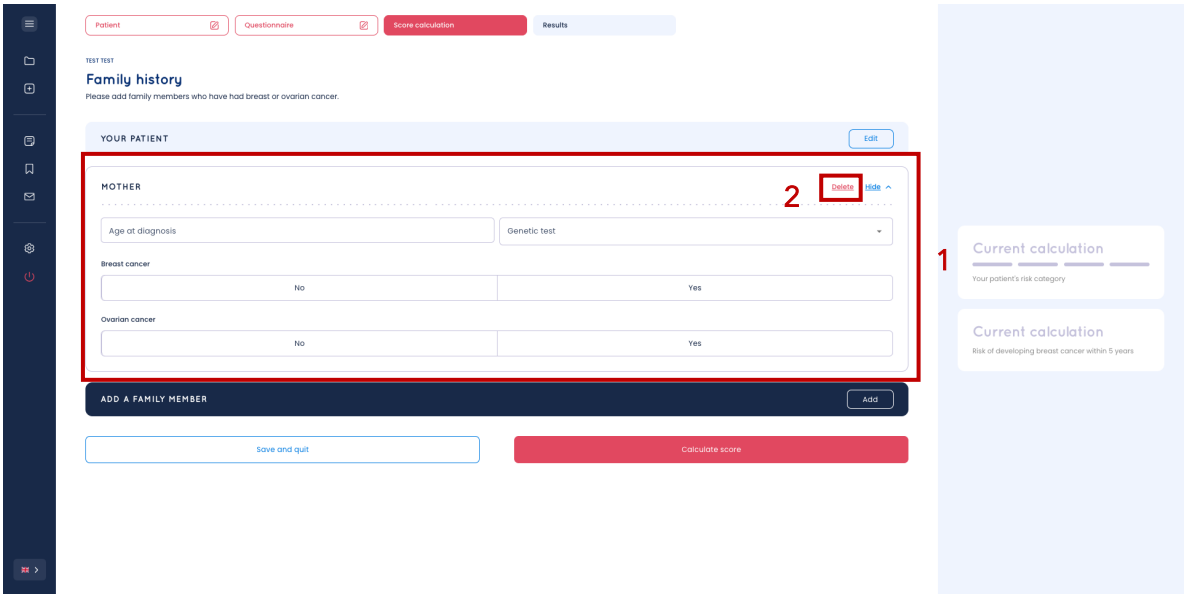
- First degree: mother, father, sister, daughter or brother.
- Paternal branch: grandmother, aunt, half-sister, cousin (aunt's daughter), cousin (uncle's daughter).
- Maternal branch: grandmother, aunt, half-sister, cousin (aunt's daughter), cousin (uncle's daughter).



When the user has selected the family member, they will have to complete the questionnaire (1). If they made a mistake when choosing the member, they can delete it by clicking on the “Delete” button (2).

For the question of age at diagnosis, if the patient does not have this information, the user can enter either the current age or the age at death.

Concerning the result of the genetic test, if it has been carried out, it must be indicated. If the patient does not know the result, “Unknown” should be selected.



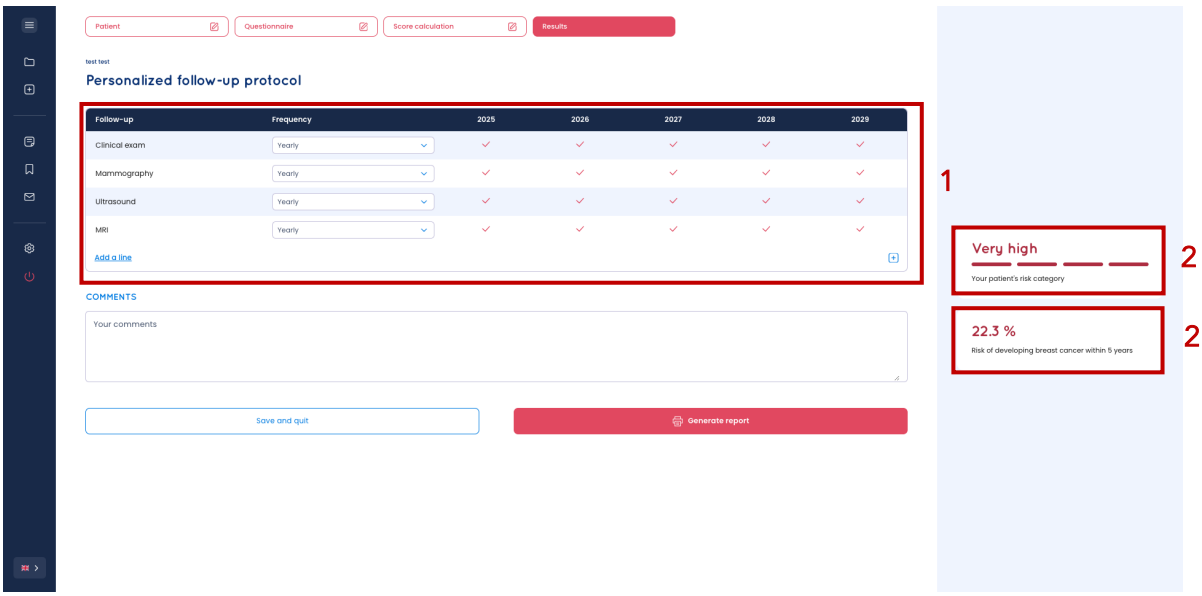
When the user has fully completed the questionnaire, they can click on “Calculate score” to assess the woman’s 5-year risk. If information such as breast density, Polygenic Risk Score, or family member information is missing, the healthcare professional can click “Save and quit ” to save the exam and the information entered while waiting for the results.

Once the results are known, the user can reselect the patient's file as well as the examination, which will have the status "In progress", in order to resume the risk assessment.

d. Risk calculation and visualization of results

When the user clicks on "Calculate score" for the patient, they will be redirected to the “Results” page displaying:

- The recommendations associated with the calculated risk score and defined by default by the healthcare professional when the account is created (1).
- The patient's risk category (moderate risk, intermediate risk, high risk, very high risk) (2).
- The patient's 5-year risk score (3).

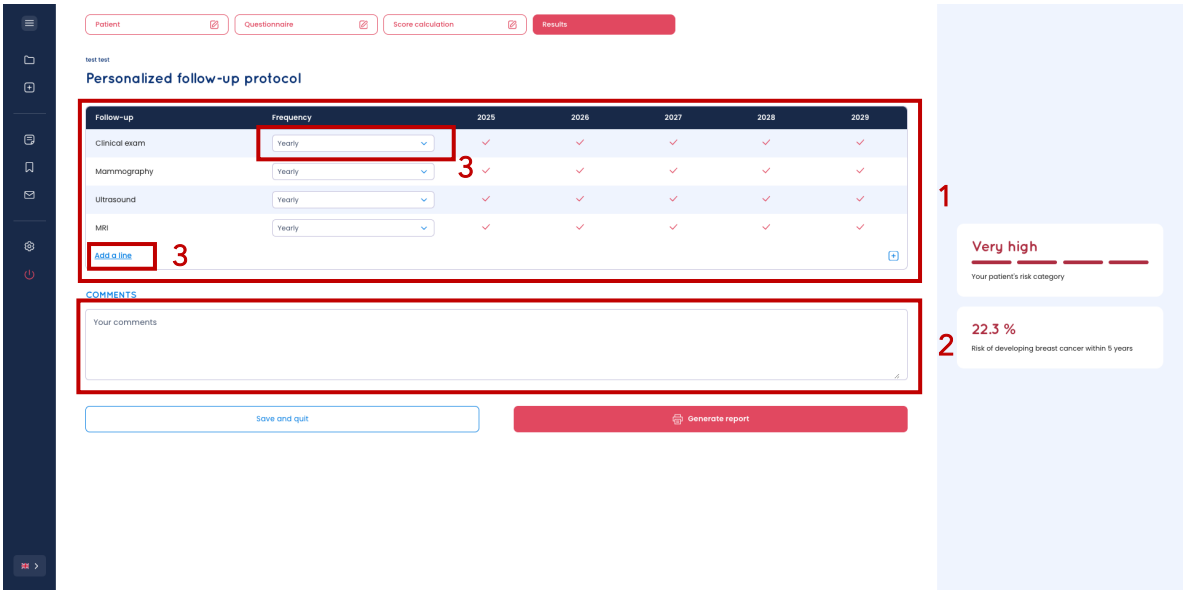


e. Recommendations

The user will access the recommendations in order to define the patient's personalized screening protocol. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a "Comments" field to add other recommendations or remarks on the patient's profile (2).

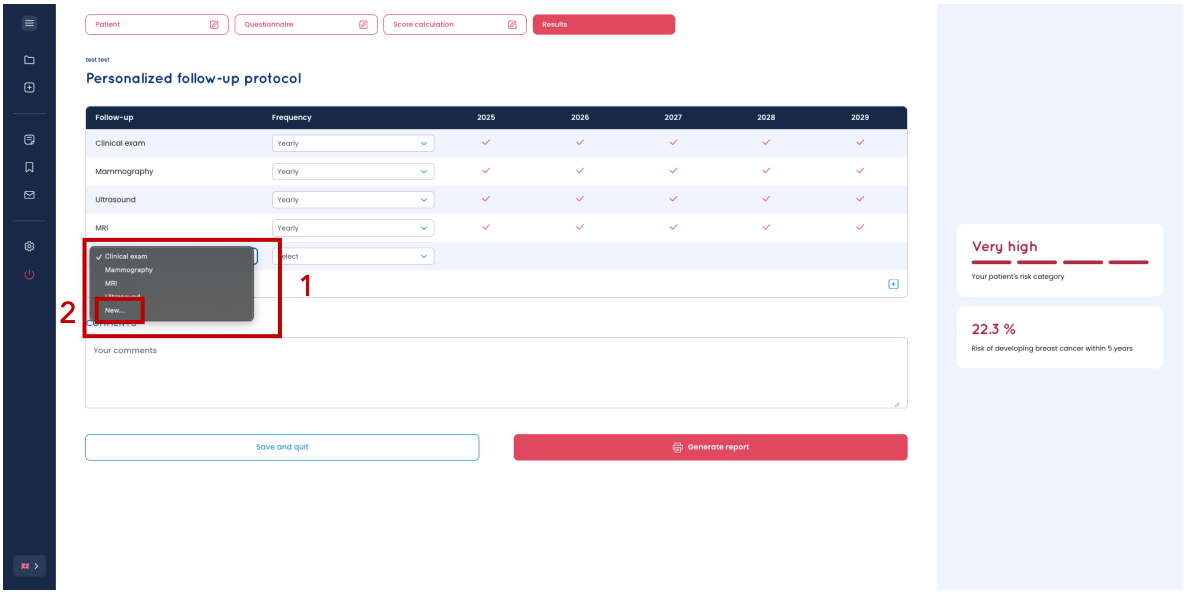
They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account.

The user can modify the frequency of examinations (3) and add more by clicking on "Add a line" (4).

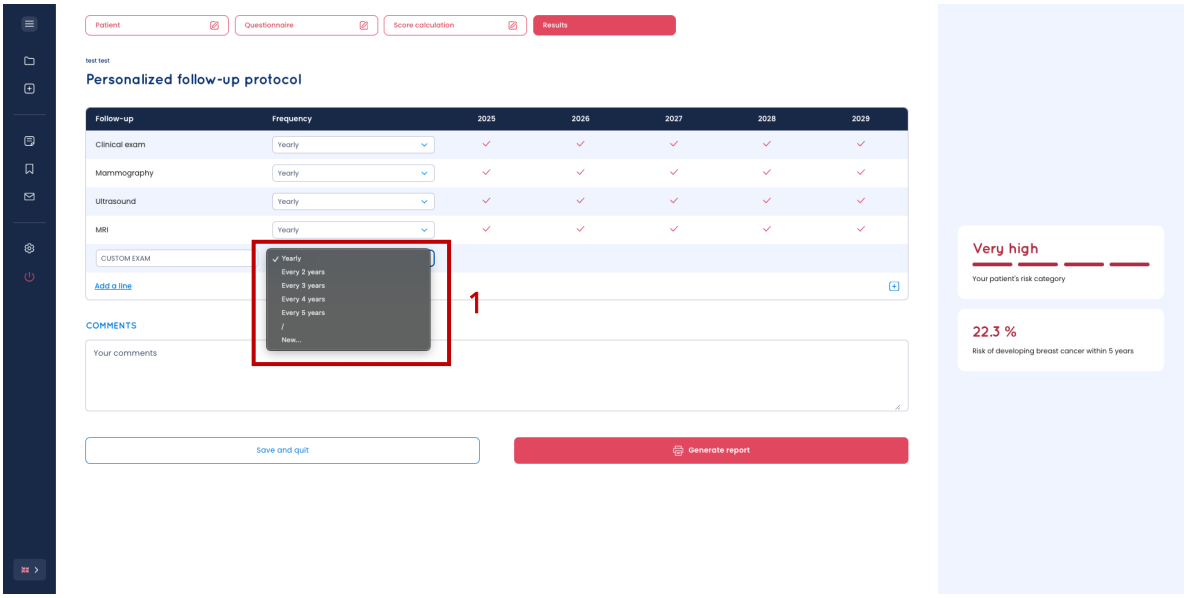


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If they wish to add an exam that is not present in the list, they can select “New” (2) and manually enter the name of the exam.



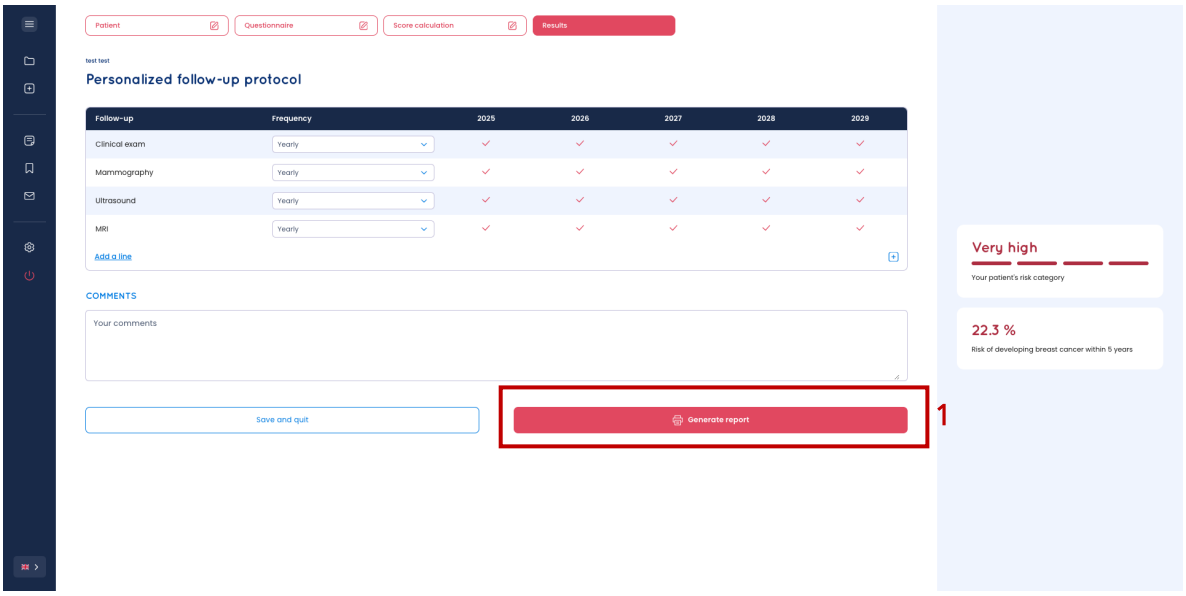
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.

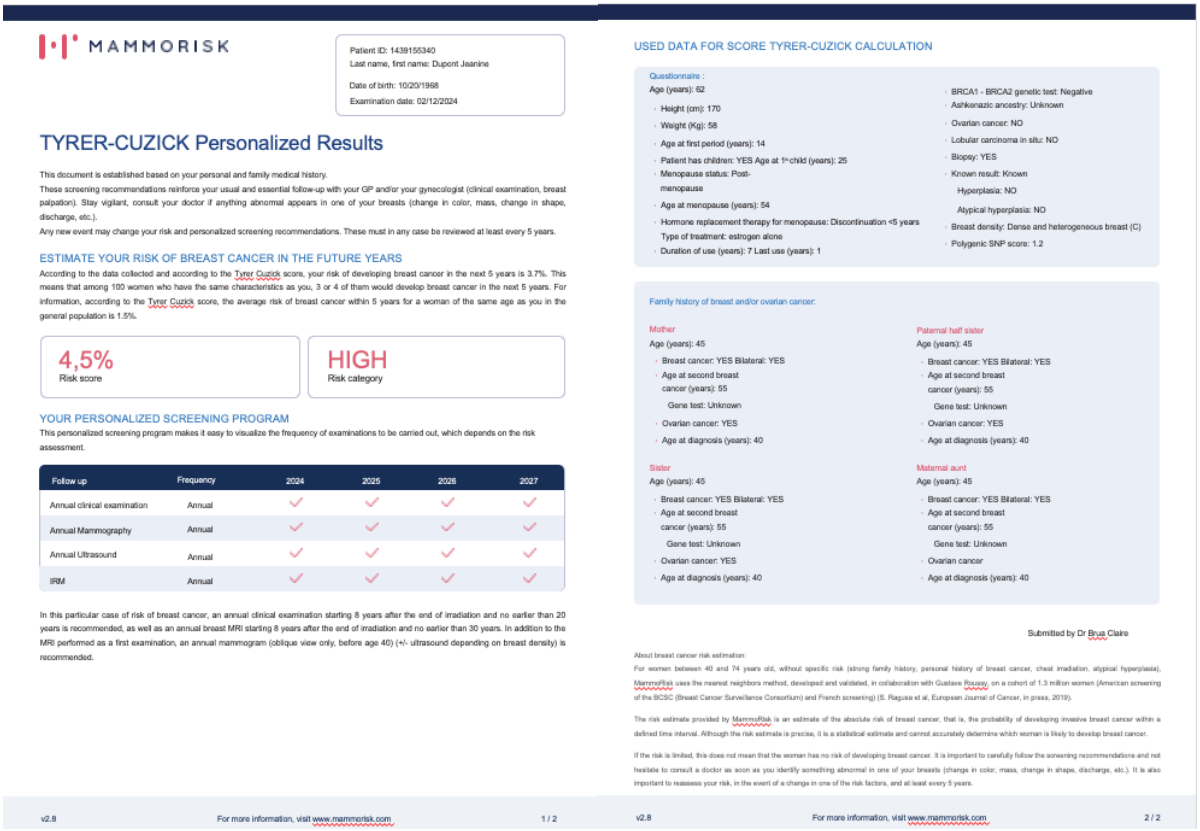


f. Generating a report

Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the "Generate report" button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional's comments.





MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine

Date of birth: 10/20/1968
Examination date: 02/12/2024

TYRER-CUZICK Personalized Results

This document is established based on your personal and family medical history.
These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in any case be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS

According to the data collected and according to the Tyrer Cuzick score, your risk of developing breast cancer in the next 5 years is 3.7%. This means that among 100 women who have the same characteristics as you, 3 or 4 of them would develop breast cancer in the next 5 years. For information, according to the Tyrer Cuzick score, the average risk of breast cancer within 5 years for a woman of the same age as you in the general population is 1.5%.

4,5%	HIGH
Risk score	Risk category

YOUR PERSONALIZED SCREENING PROGRAM

This personalized screening program makes it easy to visualize the frequency of examinations to be carried out, which depends on the risk assessment.

Follow up	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓
IRM	Annual	✓	✓	✓	✓

In this particular case of risk of breast cancer, an annual clinical examination starting 8 years after the end of irradiation and no earlier than 20 years is recommended, as well as an annual breast MRI starting 8 years after the end of irradiation and no earlier than 30 years. In addition to the MRI performed as a first examination, an annual mammogram (oblique view only, before age 40) (+/- ultrasound depending on breast density) is recommended.

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USED DATA FOR SCORE TYRER-CUZICK CALCULATION

Questionnaire :
Age (years): 62
- Height (cm): 170
- Weight (Kg): 58
- Age at first period (years): 14
- Patient has children: YES Age at 1st child (years): 25
- Menopause status: Post-menopause
- Age at menopause (years): 54
- Hormone replacement therapy for menopause: Discontinuation <5 years Type of treatment: estrogen alone
- Duration of use (years): 7 Last use (years): 1
- BRCA1 - BRCA2 genetic test: Negative
- Ashkenazic ancestry: Unknown
- Ovarian cancer: NO
- Lobular carcinoma in situ: NO
- Biopsy: YES
- Known result: Known
  - Hyperplasia: NO
  - Atypical hyperplasia: NO
- Breast density: Dense and heterogeneous breast (C)
- Polygenic SNP score: 1.2

Family history of breast and/or ovarian cancer:

Mother
Age (years): 45
- Breast cancer: YES Bilateral: YES
- Age at second breast cancer (years): 55
  - Gene test: Unknown
- Ovarian cancer: YES
- Age at diagnosis (years): 40

Paternal half sister
Age (years): 45
- Breast cancer: YES Bilateral: YES
- Age at second breast cancer (years): 55
  - Gene test: Unknown
- Ovarian cancer: YES
- Age at diagnosis (years): 40

Sister
Age (years): 45
- Breast cancer: YES Bilateral: YES
- Age at second breast cancer (years): 55
  - Gene test: Unknown
- Ovarian cancer: YES
- Age at diagnosis (years): 40

Maternal aunt
Age (years): 45
- Breast cancer: YES Bilateral: YES
- Age at second breast cancer (years): 55
  - Gene test: Unknown
- Ovarian cancer
- Age at diagnosis (years): 40

Submitted by Dr Brua Claire

About breast cancer risk estimation:
For women between 40 and 74 years old, without specific risk (strong family history, personal history of breast cancer, chest irradiation, atypical hyperplasia), MammoRisk uses the nearest neighbors method, developed and validated, in collaboration with Gustave Roussy, on a cohort of 1.3 million women (American screening of the BCSC (Breast Cancer Surveillance Consortium) and French screening) (S. Ragusa et al, European Journal of Cancer, in press, 2019).

The risk estimate provided by MammoRisk is an estimate of the absolute risk of breast cancer, that is, the probability of developing invasive breast cancer within a defined time interval. Although the risk estimate is precise, it is a statistical estimate and cannot accurately determine which woman is likely to develop breast cancer.

If the risk is limited, this does not mean that the woman has no risk of developing breast cancer. It is important to carefully follow the screening recommendations and not hesitate to consult a doctor as soon as you identify something abnormal in one of your breasts (change in color, mass, change in shape, discharge, etc.). It is also important to reassess your risk, in the event of a change in one of the risk factors, and at least every 5 years.

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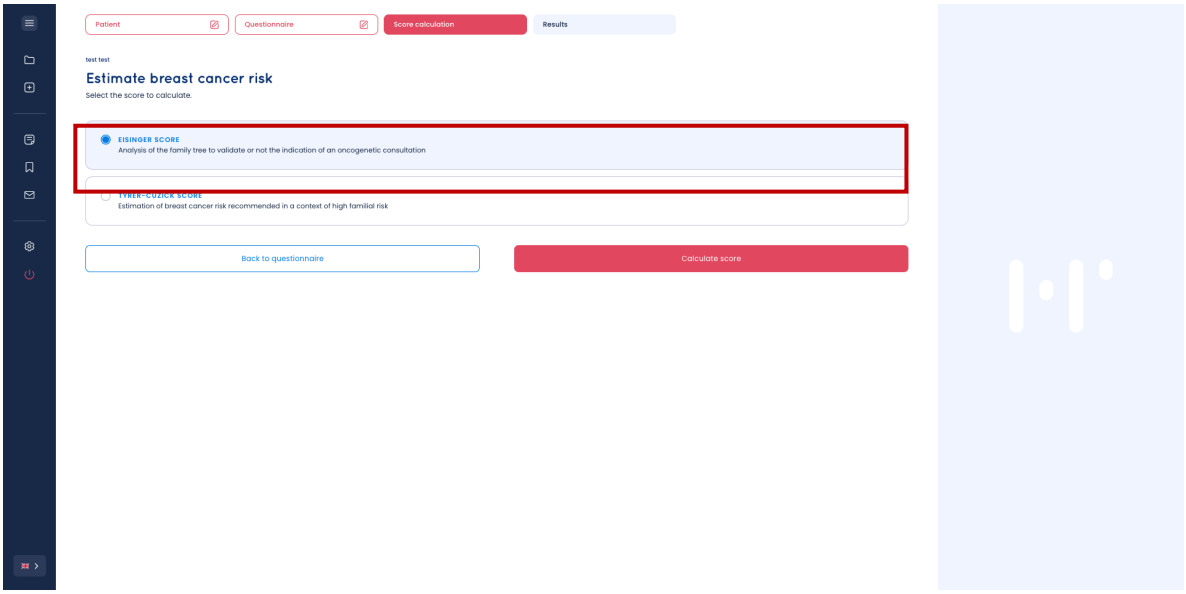
3. Eisinger score

a. Presentation

The Eisinger score is a pedigree analysis score to validate the indication for a genetic counseling and to consider mutation screening.

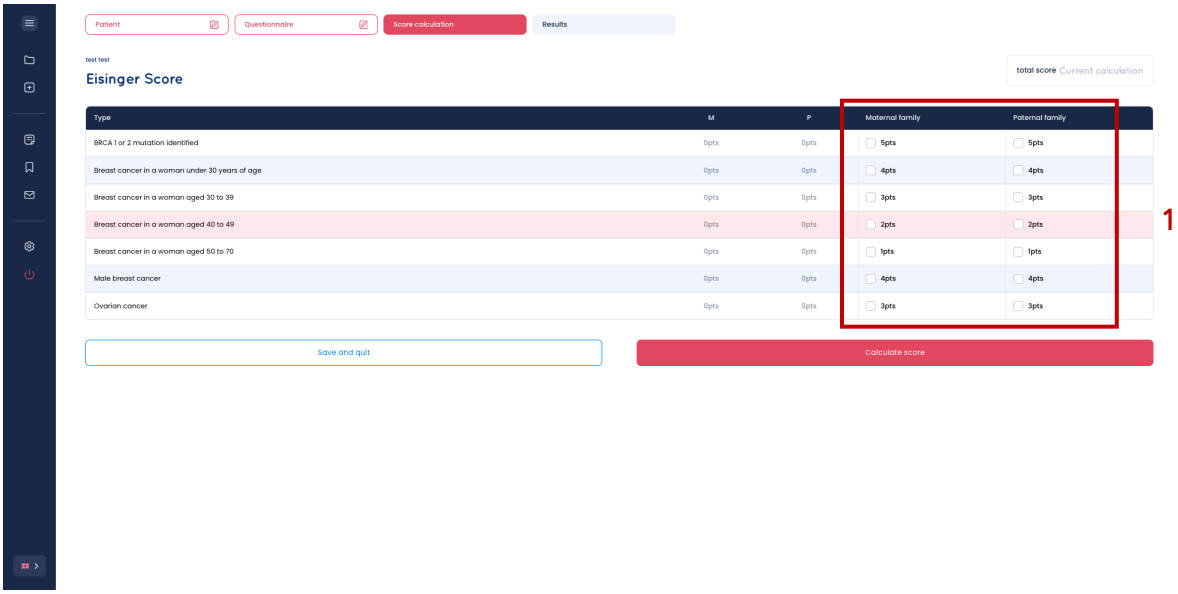
Risk score calculation: The Eisinger score is calculated by assigning points to certain personal and family histories (maternal and paternal lines) of breast and/or ovarian cancer. The sum of the points helps determine the indication for referral to genetic counseling and to consider screening for mutations.

⚠ This score is only accessible to healthcare professionals practicing in France.



b. Questionnaire

The user must check the boxes corresponding to the patient's family history according to the family branch (maternal or paternal). (1)

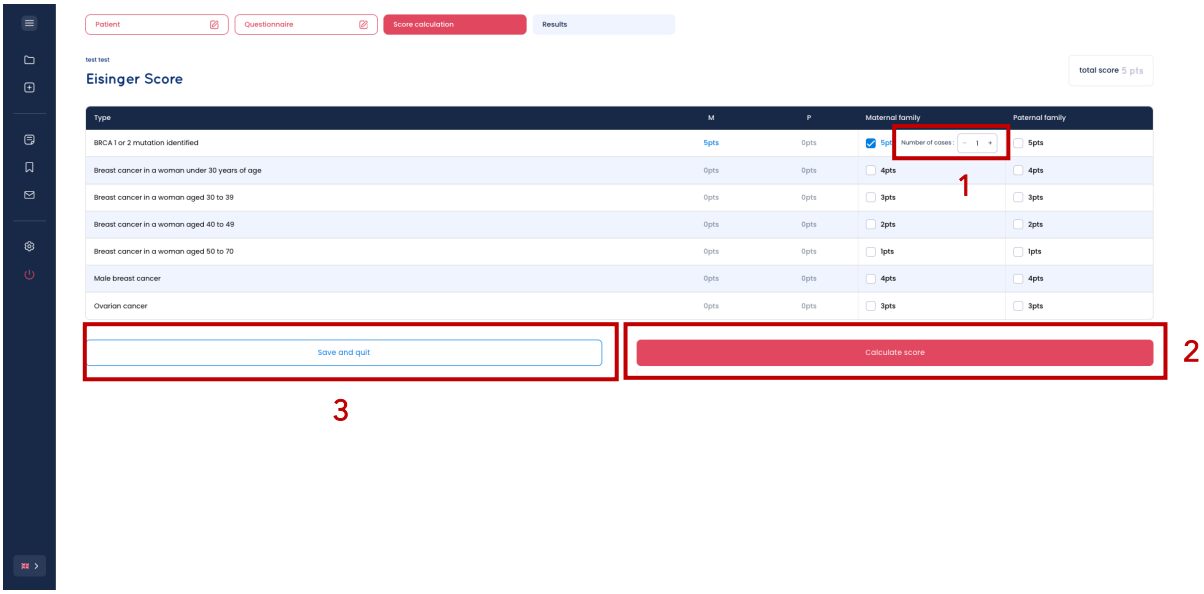


Once the box is checked, it must indicate the number of occurrences within the family. To do this, they can use box (1) and add the number of people concerned by clicking on the "+" button.

If the user has added too many backgrounds, they can click the "-" button to remove some. If the user has selected a type of history by mistake, they can uncheck it so that it is not taken into account in the risk calculation.

Once the user has fully completed the questionnaire, they can click on “Calculate score” (2) to calculate the need to refer the patient to a genetic counseling. If information is missing regarding family history, the healthcare professional can click “Save and quit” (3) to save the exam and the information entered until this data becomes available.

Once all the data are known, they can reselect the patient's file as well as the examination, which will have the status "In progress", in order to resume the calculation.



c. Risk calculation and visualization of results

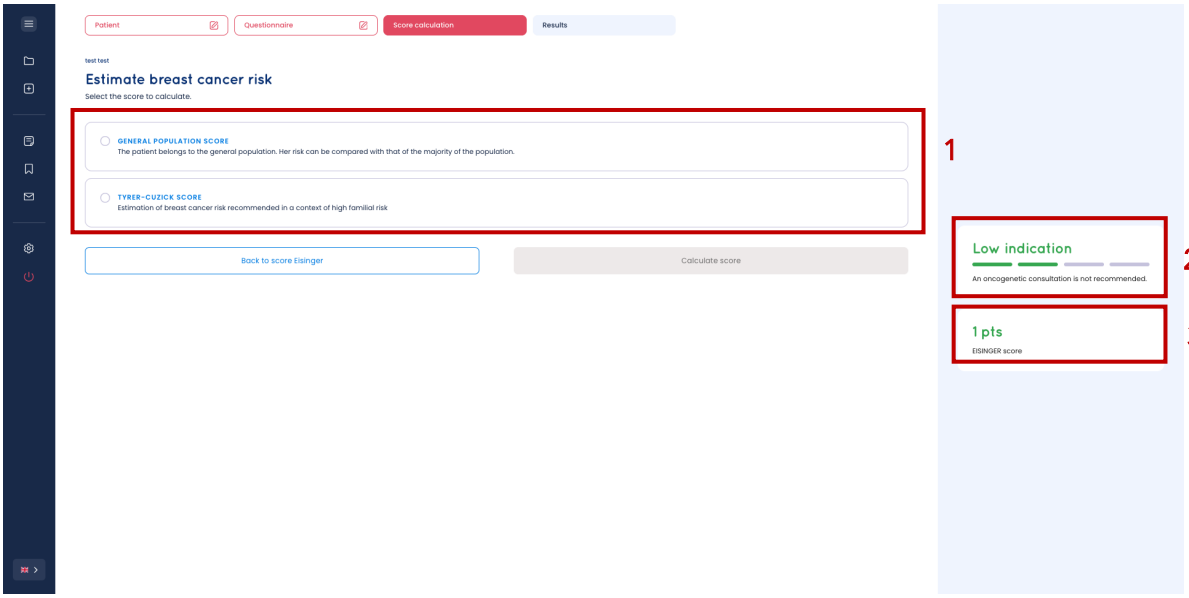
When the user clicks on “Calculate the score” of the patient, they will be redirected to the “Results” page displaying the following scenarios:

- **If the Eisinger score is less than 3:**

o Referral for another score, as the patient does not need to attend a genetic counseling (1). The user can then choose the general population risk score or the Tyrer-Cuzick score.

o Weak indication for a genetic counseling (2).

o Eisinger score value (3).

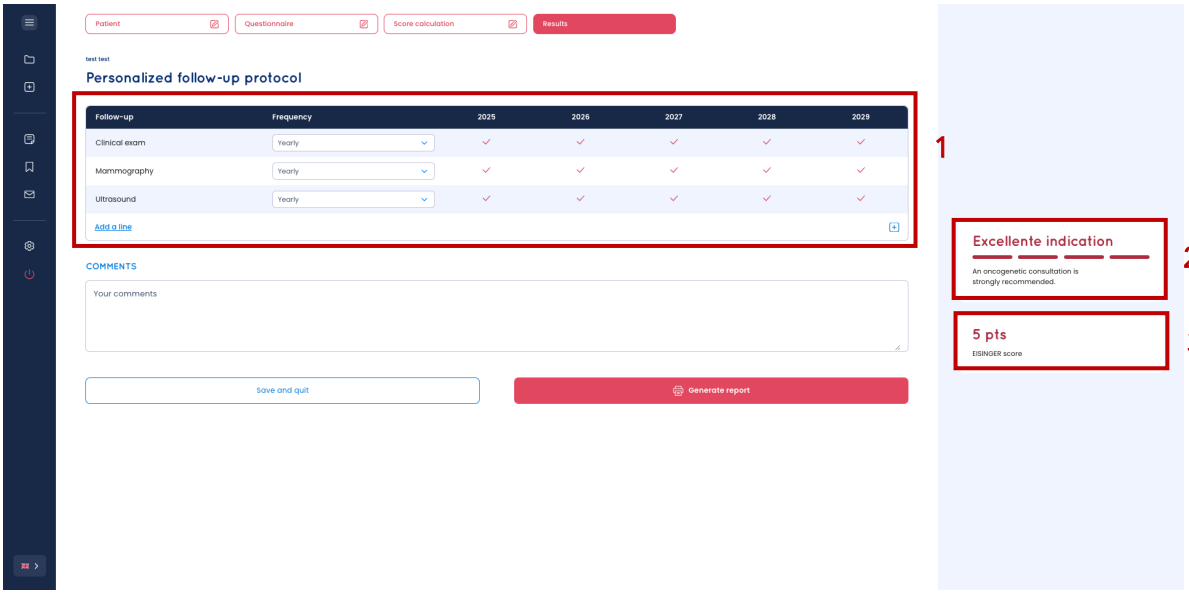


- If the Eisinger score is greater than or equal to 3:

  o The recommendations associated with the calculated risk score and defined by default by the healthcare professional when the account was created. (1).

  o Possible or excellent Indication for a genetic counseling (2).

  o Eisinger score value (3).

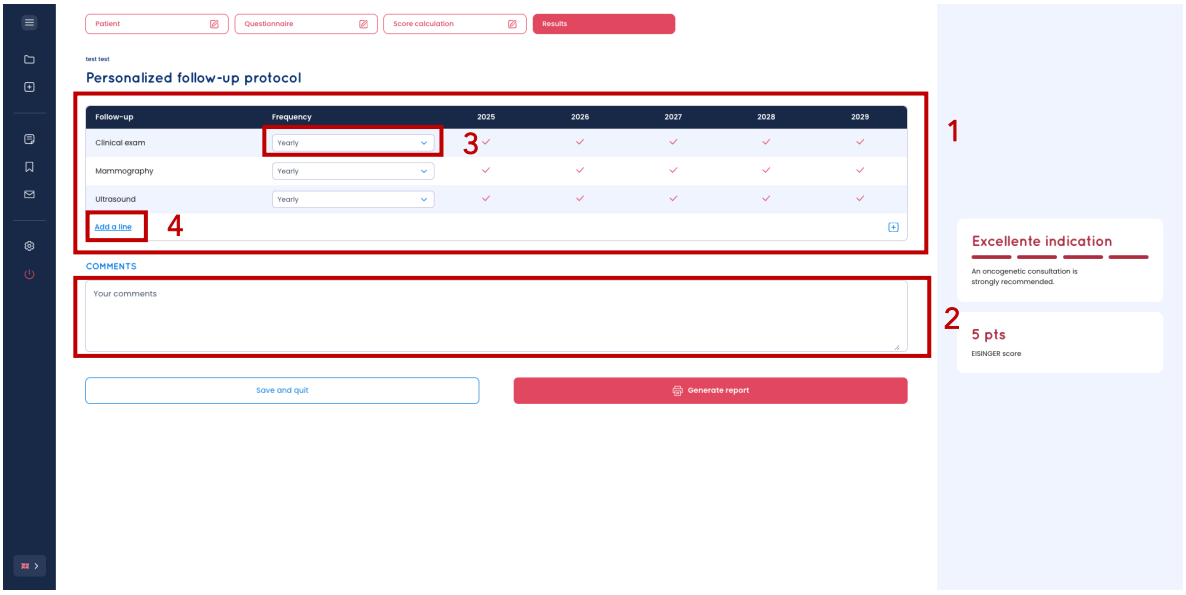


d. Recommendations

The user will access the recommendations in order to define the personalized monitoring protocol for the patient while awaiting the results of the genetic counseling. It will have a table of recommendations including the examinations types and their monitoring frequencies (1), as well as a "Comments" field to add other recommendations or remarks on the patient's profile (2).

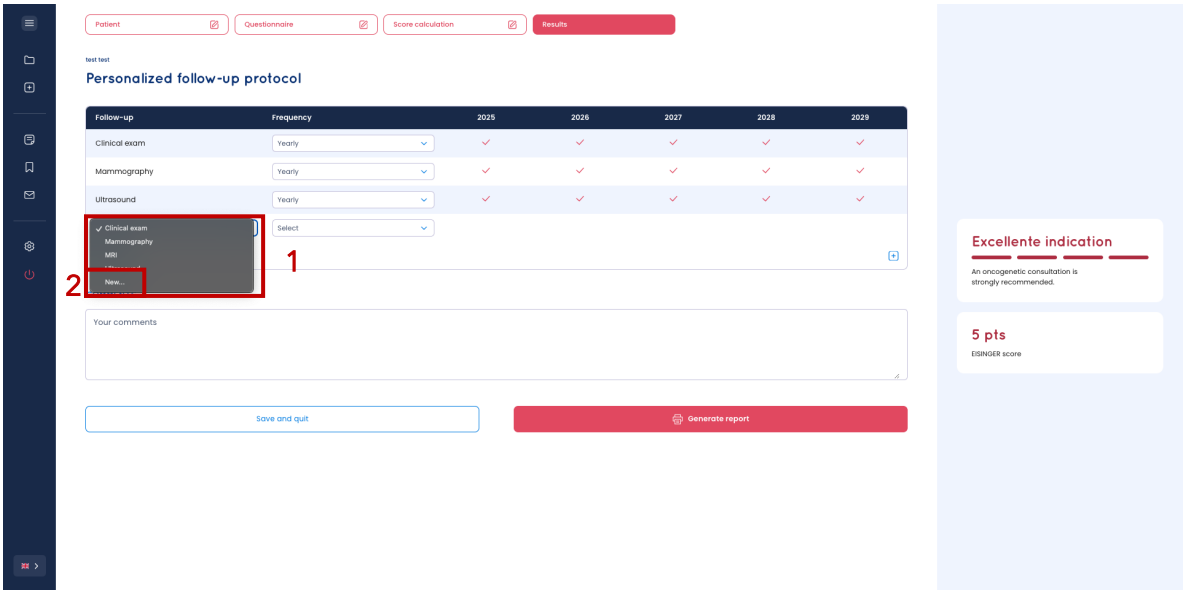
They will then be able to select the exams to be implemented. The recommendations displayed are those defined by default by the healthcare professional when setting up the account.

The user can modify the frequency of examinations (3) and add more by clicking on "Add a line" (4).

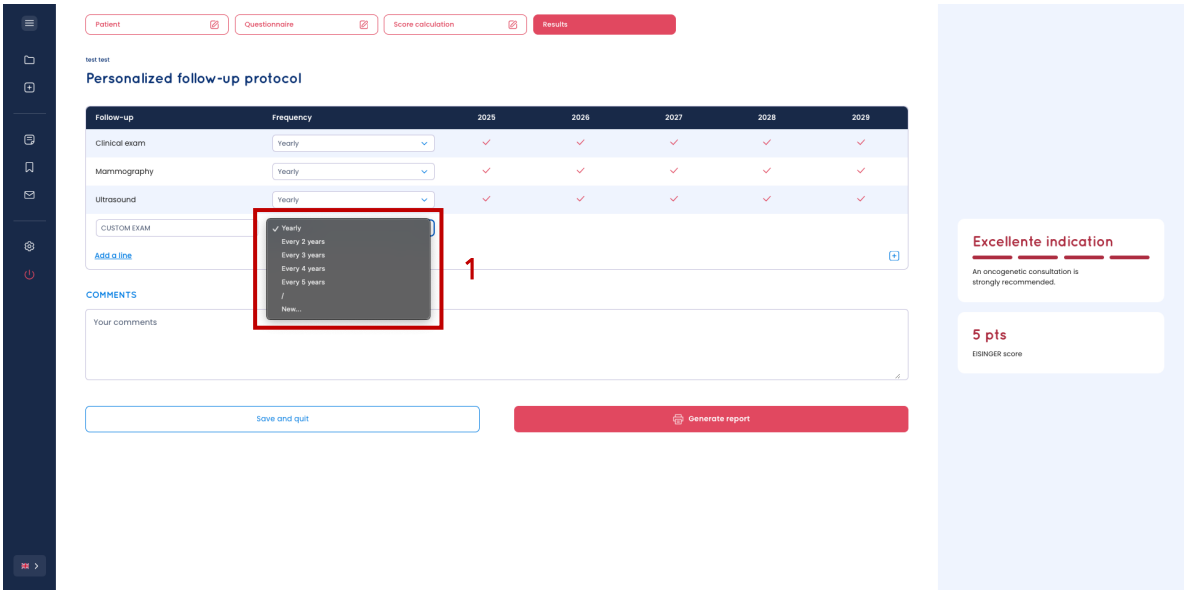


Once the user adds a new line to indicate an additional exam, they must select the exam type (1).

If they wish to add an exam that is not present in the list, they can select "New" (2) and manually enter the name of the exam.



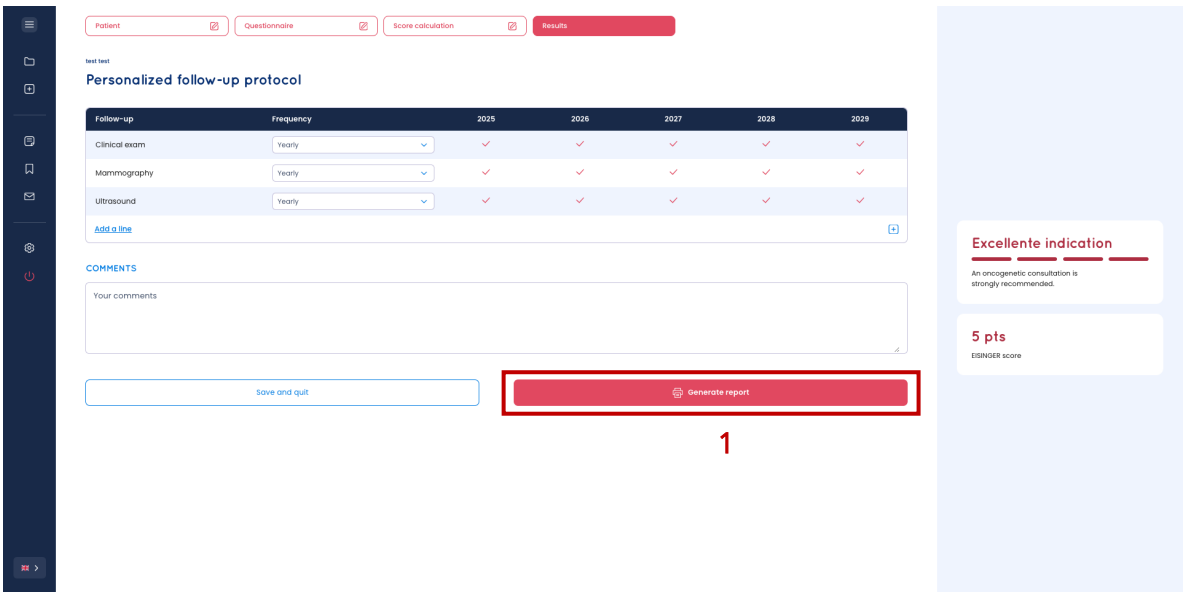
Once the exam has been added, the user will need to define its frequency by clicking on the corresponding drop-down menu (1). The row will then display the exam with its recommendation and frequency in the table.

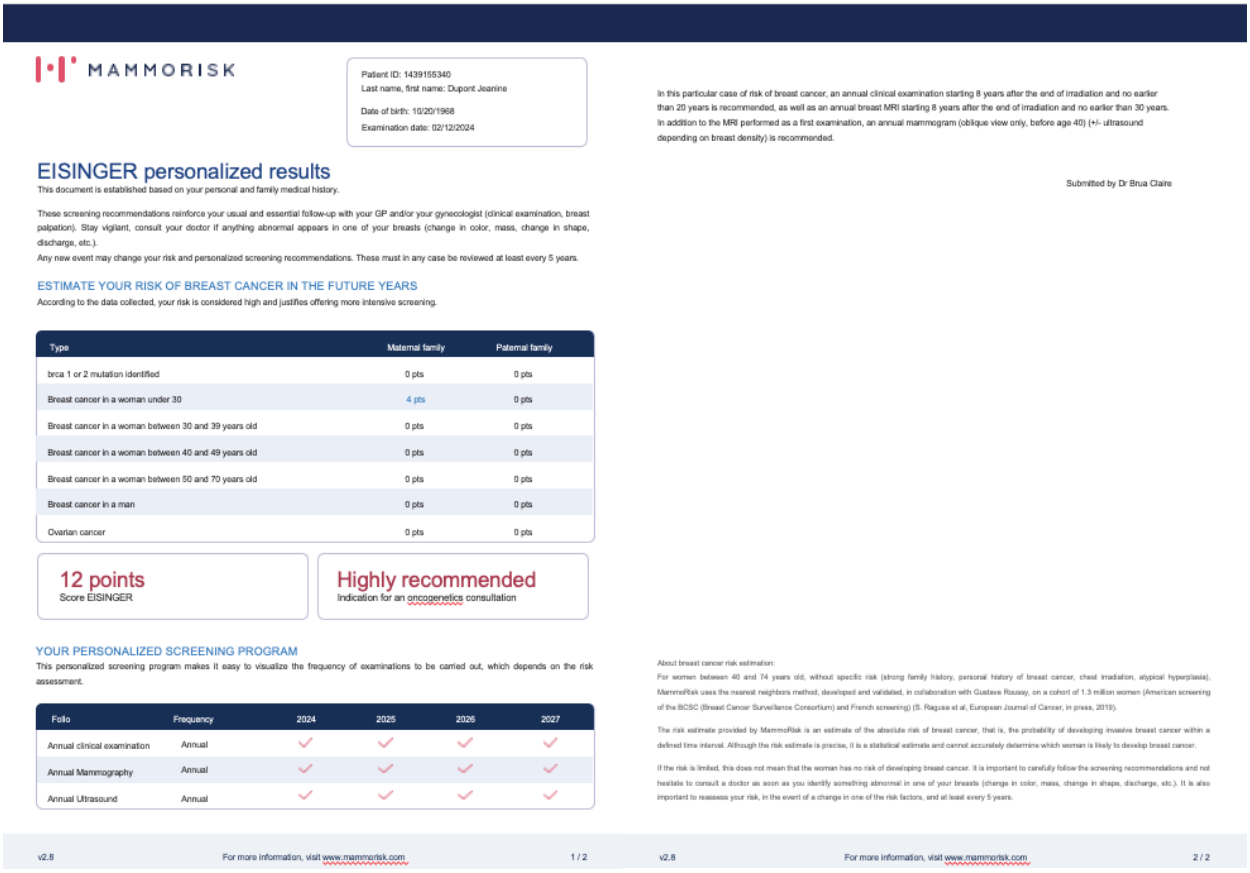


e. Generating a report

Once the user has defined the personalized monitoring protocol as well as his comments, they can generate the report by clicking on the "Generate report" button (1). The generated report can be downloaded in PDF format.

A new tab will open with the patient's report, summarizing the protocol as well as the healthcare professional's comments.





MAMMORISK

Patient ID: 1439155340
Last name, first name: Dupont Jeanine
Date of birth: 10/20/1968
Examination date: 02/12/2024

EISINGER personalized results

This document is established based on your personal and family medical history.

These screening recommendations reinforce your usual and essential follow-up with your GP and/or your gynecologist (clinical examination, breast palpation). Stay vigilant, consult your doctor if anything abnormal appears in one of your breasts (change in color, mass, change in shape, discharge, etc.).
Any new event may change your risk and personalized screening recommendations. These must in any case be reviewed at least every 5 years.

ESTIMATE YOUR RISK OF BREAST CANCER IN THE FUTURE YEARS

According to the data collected, your risk is considered high and justifies offering more intensive screening.

Type	Maternal family	Paternal family
brca 1 or 2 mutation identified	0 pts	0 pts
Breast cancer in a woman under 30	4 pts	0 pts
Breast cancer in a woman between 30 and 39 years old	0 pts	0 pts
Breast cancer in a woman between 40 and 49 years old	0 pts	0 pts
Breast cancer in a woman between 50 and 70 years old	0 pts	0 pts
Breast cancer in a man	0 pts	0 pts
Ovarian cancer	0 pts	0 pts

12 points
Score EISINGER

Highly recommended
Indication for an oncogenetics consultation

YOUR PERSONALIZED SCREENING PROGRAM

This personalized screening program makes it easy to visualize the frequency of examinations to be carried out, which depends on the risk assessment.

Follo	Frequency	2024	2025	2026	2027
Annual clinical examination	Annual	✓	✓	✓	✓
Annual Mammography	Annual	✓	✓	✓	✓
Annual Ultrasound	Annual	✓	✓	✓	✓

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In this particular case of risk of breast cancer, an annual clinical examination starting 8 years after the end of irradiation and no earlier than 20 years is recommended, as well as an annual breast MRI starting 8 years after the end of irradiation and no earlier than 30 years. In addition to the MRI performed as a first examination, an annual mammogram (oblique view only, before age 40) (+/- ultrasound depending on breast density) is recommended.

Submitted by Dr Brua Claire

About breast cancer risk estimation:
For women between 40 and 74 years old, without specific risk (strong family history, personal history of breast cancer, chest irradiation, atypical hyperplasia), MammoRisk uses the nearest neighbors method, developed and validated, in collaboration with Gustave Roussy, on a cohort of 1.3 million women (American screening of the BCSC (Breast Cancer Surveillance Consortium) and French screening) (S. Ragusa et al, European Journal of Cancer, in press, 2019).

The risk estimate provided by MammoRisk is an estimate of the absolute risk of breast cancer, that is, the probability of developing invasive breast cancer within a defined time interval. Although the risk estimate is precise, it is a statistical estimate and cannot accurately determine which woman is likely to develop breast cancer.

If the risk is limited, this does not mean that the woman has no risk of developing breast cancer. It is important to carefully follow the screening recommendations and not hesitate to consult a doctor as soon as you identify something abnormal in one of your breasts (change in color, mass, change in shape, discharge, etc.). It is also important to reassess your risk, in the event of a change in one of the risk factors, and at least every 5 years.

v2.8 For more information, visit www.mammorisk.com 2 / 2

IX. Maintenance

1. Security updates and patches

This online application is continuously maintained by a dedicated team at the manufacturer. All security updates, patches, and performance improvements are managed centrally and applied automatically during scheduled maintenance windows. This ensures that users always have access to the most secure and up-to-date version of the software. In case of any issues related to security updates or require further information, please contact the support team (see Contact section).

2. Data backup and feature restoration

All data backup and feature restoration processes are managed by a dedicated team at the manufacturer. Regular backups are performed automatically to maintain data integrity and ensure system continuity. For further assistance or inquiries, please contact the support team (see Contact section).

3. User role (privileges)

The application assigns standard user privileges necessary for performing tasks related to risk assessments. All users have access only to the features required for their tasks. For security and confidentiality reasons, detailed information about internal role management is not disclosed. In case of any questions regarding the access rights, please contact the support team (see Contact section).

4. Fail safe mode use

This software does not incorporate a dedicated fail-safe mode function. In the event of a software issue or malfunction, please contact the support team immediately (see Contact section).

5. Information about logging

Among the logs maintained on the cloud side of the software, connection and usage logs (for billing purposes) are recorded. These logs capture key application events, errors, and user activities. Access to this logging data is restricted to authorized personnel for troubleshooting, billing and audit purposes and is not available to end users. For any inquiries regarding logging, please contact the support team (see Contact section).

X. Appendices

Appendix 1: Related scientifics publications

Scientific papers:

- Stephane Ragusa et al, A new non-parametric breast cancer risk- assessment model developed on a US cohort and validated on European screening populations: Performance and potential use for stratification (in press, European Journal of Cancer).
- Weigert J, Cavanaugh N, Ju T. Evaluating Mammographer Acceptance of MammoRisk Software. Radiol Technol. 2018 Mar.
- Vachon Vachon et al. The Contributions of Breast Density and Common Genetic Variation to Breast Cancer Risk. JNCI J Natl Cancer Inst (2015) 107(5): dju397
- Pharoah PD, Antoniou AC, Easton DF, Ponder BA. Polygenes, risk prediction, and targeted prevention of breast cancer. N Engl J Med. 2008
- Eleanor Roberts, Sacha Howell, D Gareth Evans. Polygenic risk scores and breast cancer risk prediction. 2023

Posters and oral communications:

- Gauthier E, et al. Breast cancer risk score: a data mining approach to improve readability. Proceedings of the 2011 International Conference on Data Mining, July 18-21, 2011, Las Vegas, Nevada, USA. CSREA Press: Athens, GA, 2011;15-21.
- Tlemsani C et al, Receipt of breast cancer risk assessment and personalized prevention information among women diagnosed with a benign breast lesion (BBL) in a One Stop Breast Unit: a prospective assessment. SABCS 2015 (poster), Cancer Res 2015
- Stephane Ragusa et al, Development and validation of a new non- parametric breast cancer risk assessment model on US and European screening population. SABCS 2016 (poster), Cancer Res 2016.

- C. Balleyguier et al, New automated image recognition-based software to evaluate 2D breast mammographic density (BMD) according to BI-RADS® Atlas Fifth Edition recommendations, ECR 2017, oral communication
- Automated qualitative assessment of 2D breast density for breast cancer risk calculation (Corinne Balleyguier et al), 8th International Breast Density and Breast Cancer Risk Assessment Workshop, SF, June 2017
- Veron L. et al, Feasibility of breast cancer risk assessment and personalized breast screening recommendations delivery in community practice: a national prospective study (poster), EBCC 2018
- Balleyguier C. et al, Feasibility of risk assessment and personalized breast screening recommendations delivery in community radiology practice: a national prospective study (NCT02997384), oral communication, ECR 2018

Appendix 2: MammoRisk indications diagram